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Support vital en soins intensifs oncologiques.
Le support ventilatoire.

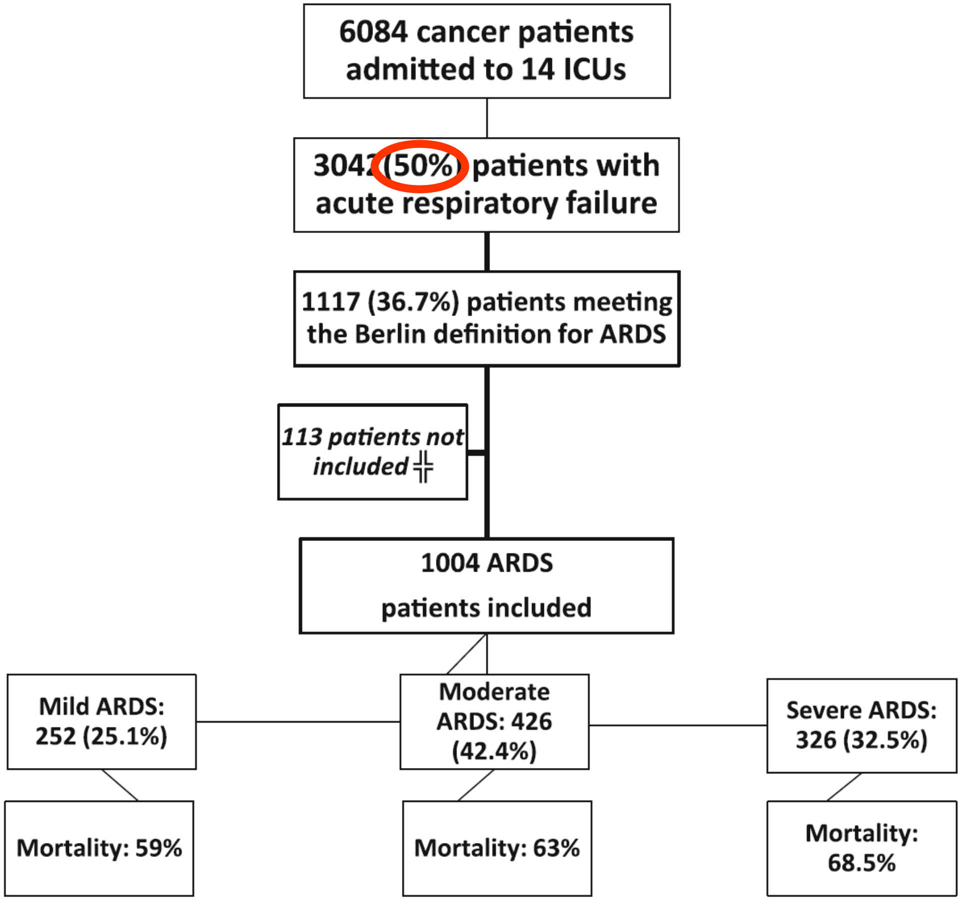
AP Meert.

ULB
iris

Conflit d’intérêt

Aucun

Epidémiologie



6084 cancer patients admitted to 14 ICUs

3042 (50%) patients with acute respiratory failure

1117 (36.7%) patients meeting the Berlin definition for ARDS

113 patients not included ‡

1004 ARDS patients included

Mild ARDS: 252 (25.1%)

Mortality: 59%

Moderate ARDS: 426 (42.4%)

Mortality: 63%

Severe ARDS: 326 (32.5%)

Mortality: 68.5%

Intensive Care Med (2014) 40:1106–1114

Etiologies

A. Les pathologies respiratoires

1. Les pneumopathies infectieuses diffuses, principalement dues à :

- Pneumocystis carinii
- Cytomégalovirus
- Aspergillose invasive
- Infections bactériennes ordinaires (Pneumocoque, Pseudomonas aeruginosa, entérobactéries,...)
- Infections virales diverses (adénovirus, virus respiratoire syncytial,...)

2. Les hémorragies

- hémorragie alvéolaire diffuse
- hémoptysie massive

3. Les atteintes néoplasiques

- obstruction et compression tumorales
- embolie de cellules tumorales et lymphangite carcinomateuse
- leucostase
- fausse déglutition et/ou fistule oesophago-respiratoire

4. Les effets toxiques du traitement

- chimiothérapie
- radiothérapie
- pneumopathie de lyse tumorale
- syndrome de l'acide rétinoïque
- pneumopathie aux leucoagglutinines
- syndrome de fuite capillaire

5. La protéinose alvéolaire secondaire

6. Les complications des greffes de moelle

- syndrome de fuite capillaire
- pneumopathie interstitielle idiopathique
- maladie veino-occlusive pulmonaire
- bronchiolite oblitérante

Table 2 ARDS causes, severity and treatment, and hospital mortality

Median (IQR) or *n* (%)	Study population ($n = 1{,}004$)	Survivors ($n = 364$)	Non-survivors ($n = 640$)	*p* value
SOFA score (31) on day-1	12 [10–13]	10 [8–12]	13 [10–13]	<0.0001
mSOFA score on day-1	9 [6–11]	7 [5–10]	9 [7–11]	<0.0001
Emergency surgery	64 (6.4 %)	34 (9.3 %)	30 (4.7 %)	0.004
Sepsis	745 (74.2 %)	275 (75.5 %)	470 (73.4 %)	0.46
Cause of ARDS				
Pulmonary infection[a]	662 (65.9 %)	281 (77.2 %)	381 (59.5 %)	<0.0001
Secondary ARDS[a]	225 (22.4 %)	55 (15.1 %)	170 (26.6 %)	<0.0001
Fungal infection[b]	293 (30.7 %)	83 (23.2 %)	210 (35.1 %)	0.0001
Pneumocystis	64 (6.4 %)	30 (8.2 %)	34 (5.3 %)	0.07
No definite diagnosis[c]	41 (5.7 %)	12 (4.5 %)	29 (6.4 %)	0.29
Berlin categories				
Mild (P/F >200)	252 (25.1 %)	103 (28.3 %)	149 (23.3 %)	
Moderate (P/F 100–200)	426 (42.4 %)	158 (43.4 %)	268 (41.8 %)	0.06
Severe (P/F < 100)	326 (32.5 %)	103 (28.3 %)	223 (34.8 %)	
Organ Support				
NIV	387 (38.6 %)	174 (47.8 %)	213 (33.3 %)	<0.0001
NIV failure	276 (27.5 %)	103 (28.3 %)	173 (27.0 %)	0.67
Endotracheal MV	893 (88.9 %)	293 (80.5 %)	600 (93.8 %)	<0.0001
Vasopressors	731 (72.8 %)	241 (66.2 %)	490 (76.6 %)	0.0004
Renal replacement therapy	306 (30.5 %)	99 (27.2 %)	207 (32.3 %)	0.09

Intensive Care Med (2014) 40:1106–1114

Diagnostic

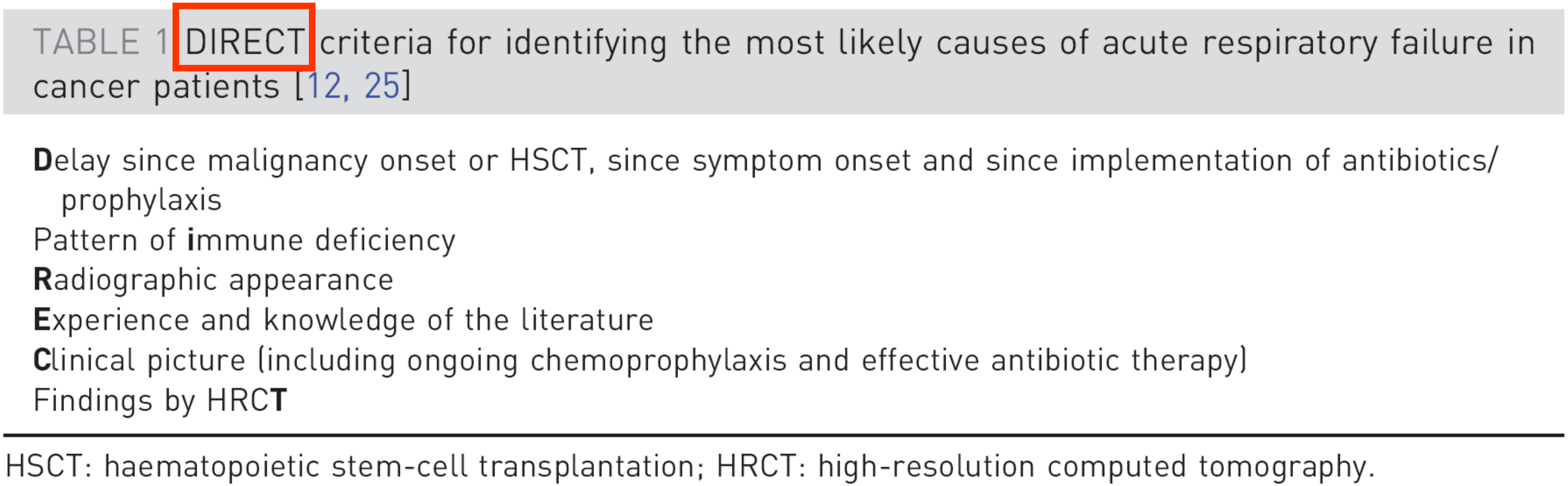


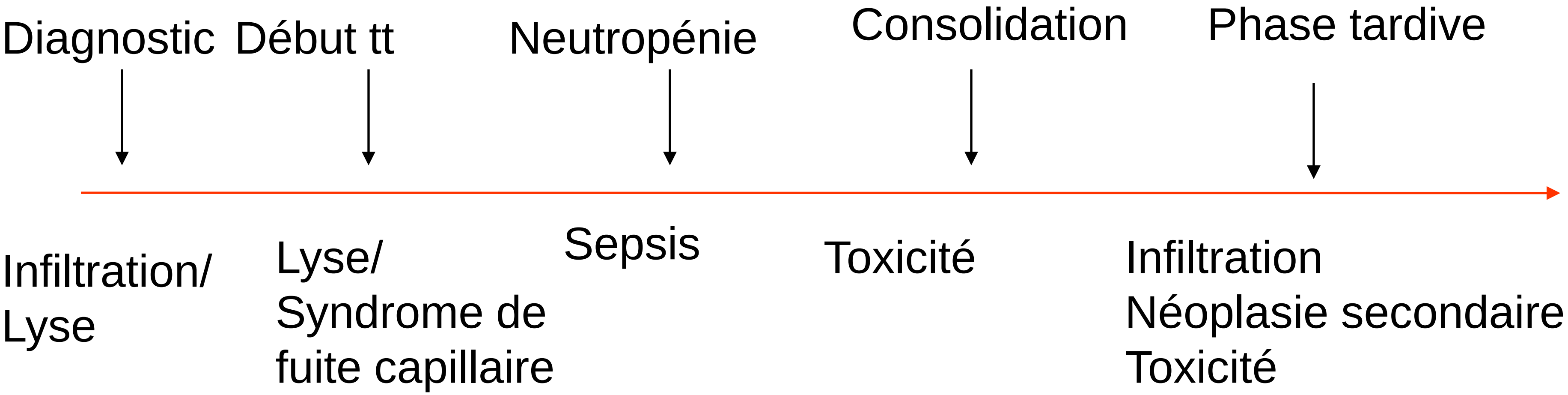
TABLE 1 DIRECT criteria for identifying the most likely causes of acute respiratory failure in cancer patients [12, 25]

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

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

Eur Respir J 2013; 42: 435–443

Causes d'IRA selon le Délai dans les hémopathies malignes



Diagnostic

Infiltration/
Lyse

Début tt

Lyse/
Syndrome de
fuite capillaire

Neutropénie

Sepsis

Consolidation

Toxicité

Phase tardive

Infiltration
Néoplasie secondaire
Toxicité

Hémorragie alvéolaire-Surcharge-Infections

Azoulay E, 2008, Rev Mal Respir

Pronostic

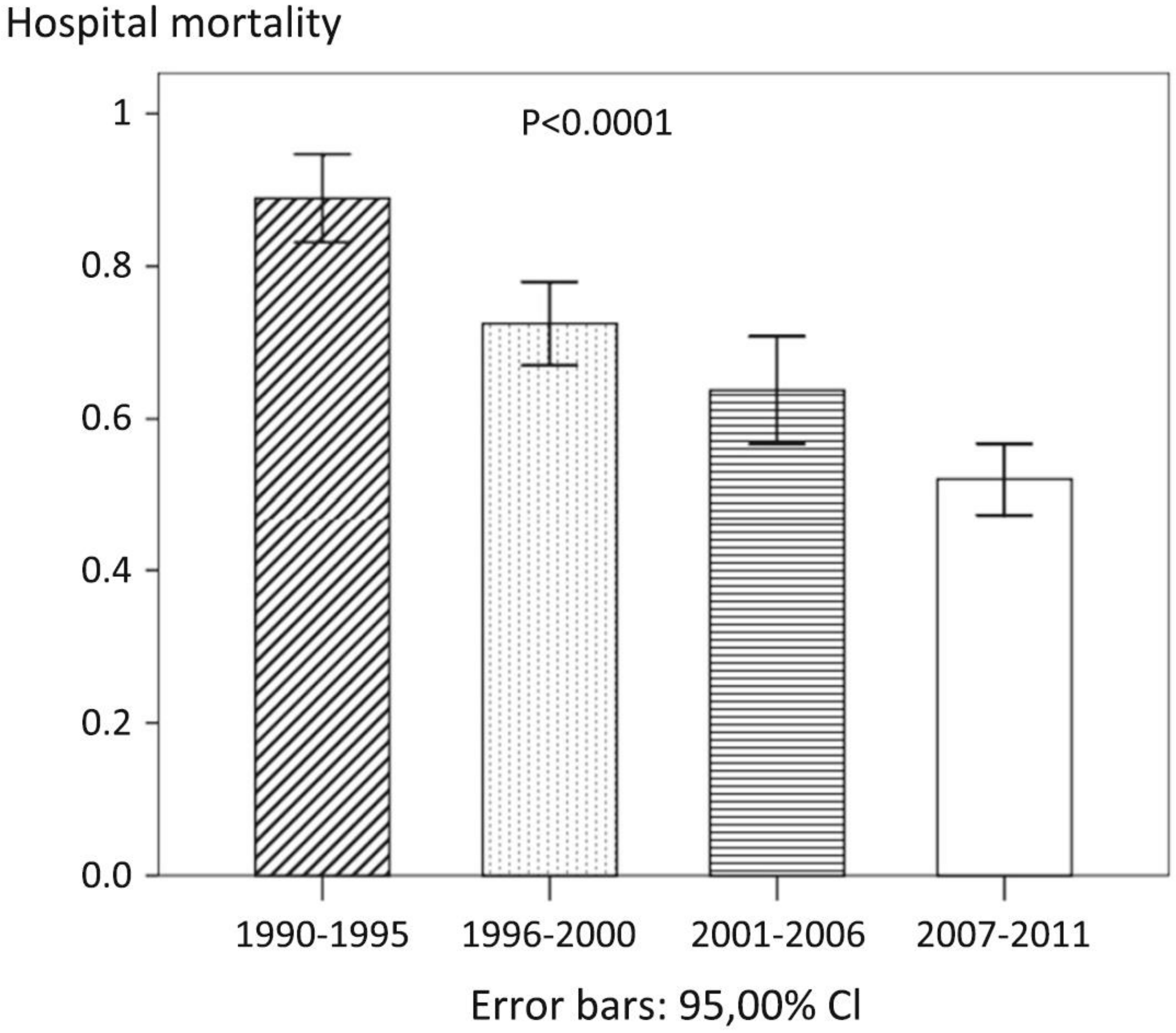
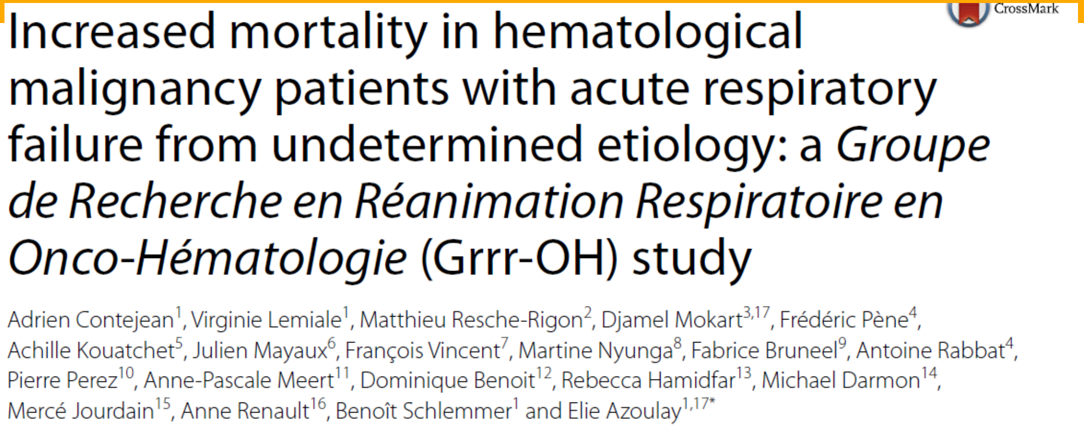


Fig. 2 Hospital mortality according to period of admission to the intensive care unit

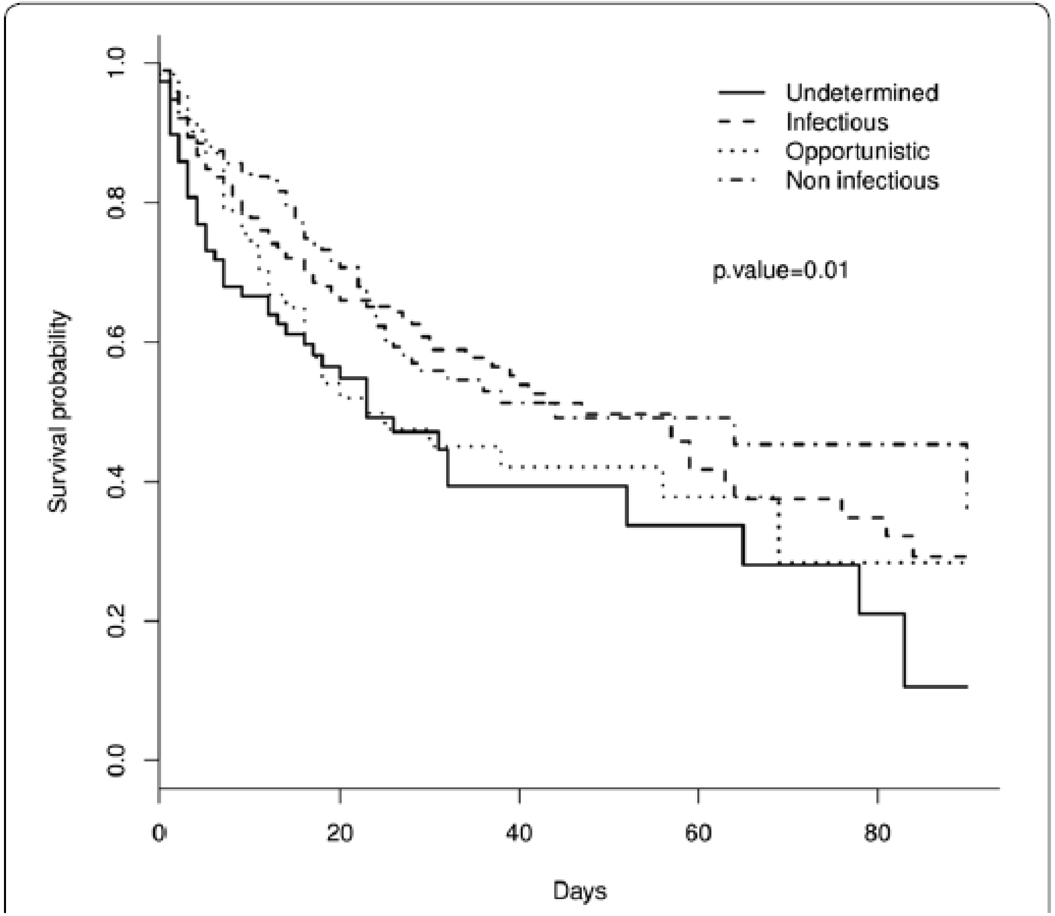
Intensive Care Med (2014) 40:1106–1114


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

Adrien Contejean[1], Virginie Lemiale[1], Matthieu Resche-Rigon[2], Djamel Mokart[3,17], Frédéric Pène[4], Achille Kouatchet[5], Julien Mayaux[6], François Vincent[7], Martine Nyunga[8], Fabrice Bruneel[9], Antoine Rabbat[4], Pierre Perez[10], Anne-Pascale Meert[11], Dominique Benoit[12], Rebecca Hamidfar[13], Michael Darmon[14], Mercé Jourdain[15], Anne Renault[16], Benoît Schlemmer[1] and Elie Azoulay[1,17*]

Mortalité hospitalière 42%

13% ARF indéterminé (mortalité 59%)



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

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

Adrien Contejean[1], Virginie Lemiale[1], Matthieu Resche-Rigon[2], Djamel Mokart[3,17], Frédéric Pène[4], Achille Kouatchet[5], Julien Mayaux[6], François Vincent[7], Martine Nyunga[8], Fabrice Bruneel[9], Antoine Rabbat[4], Pierre Perez[10], Anne-Pascale Meert[11], Dominique Benoit[12], Rebecca Hamidfar[13], Michael Darmon[14], Mercé Jourdain[15], Anne Renault[16], Benoît Schlemmer[1] and Elie Azoulay[1,17*]

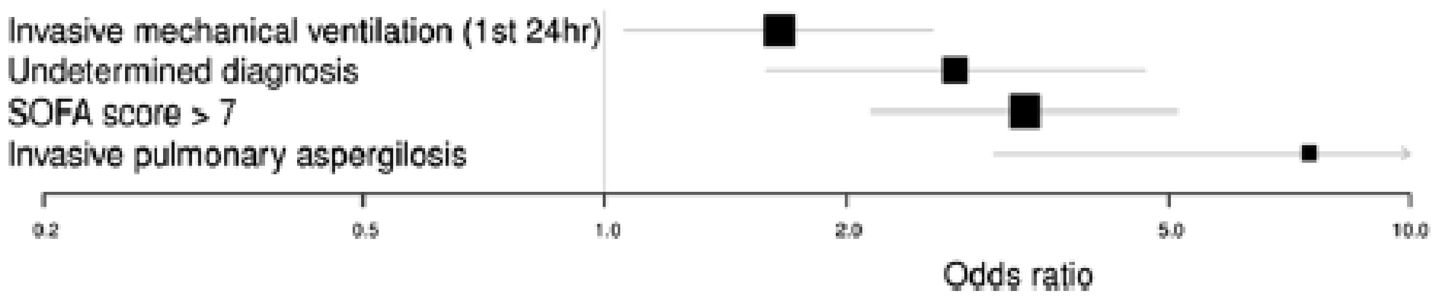


Fig. 4 Multivariable analysis of risk factors for hospital mortality. *Box* size is proportional to the accuracy of the estimate. A selection procedure was performed using a backward algorithm with a stopping criteria defined by *p* values below 0.05 for all variables included in the model. Goodness-of-fit test of the final model was checked using the le Cessie–van Houwelingen test statistic

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

Pronostic dans l'ARDS

Hospital mortality 64 %

59, 63 and 68.5 % respectively

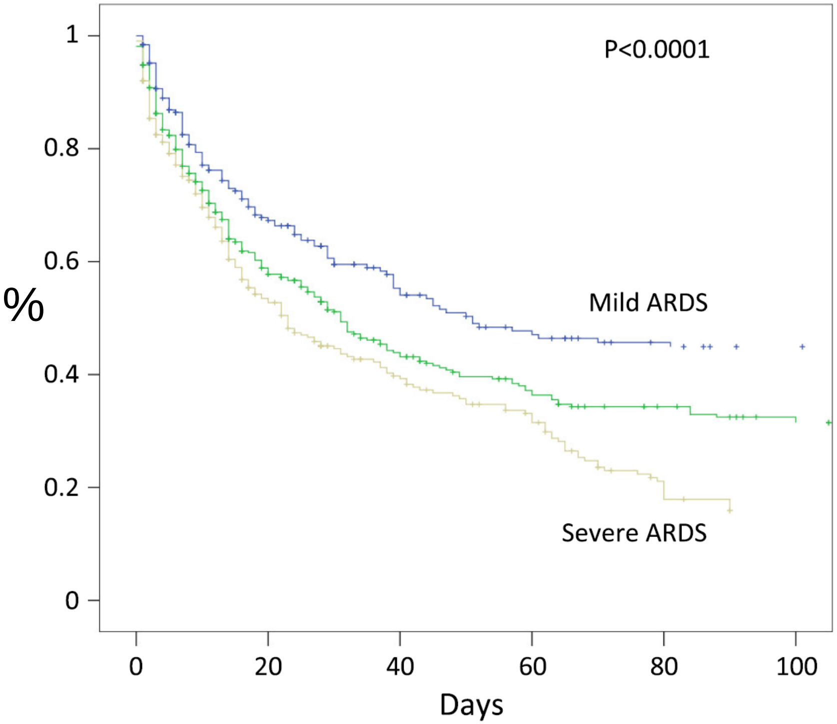


Fig. 3 Cumulative survival according to ARDS severity category in the Berlin definition. The *blue line* indicates mild ARDS, *red line* moderate ARDS and *gray line* severe ARDS. The three groups were compared using the log-rank test ($p < 0.0001$)

Intensive Care Med (2014) 40:1106–1114

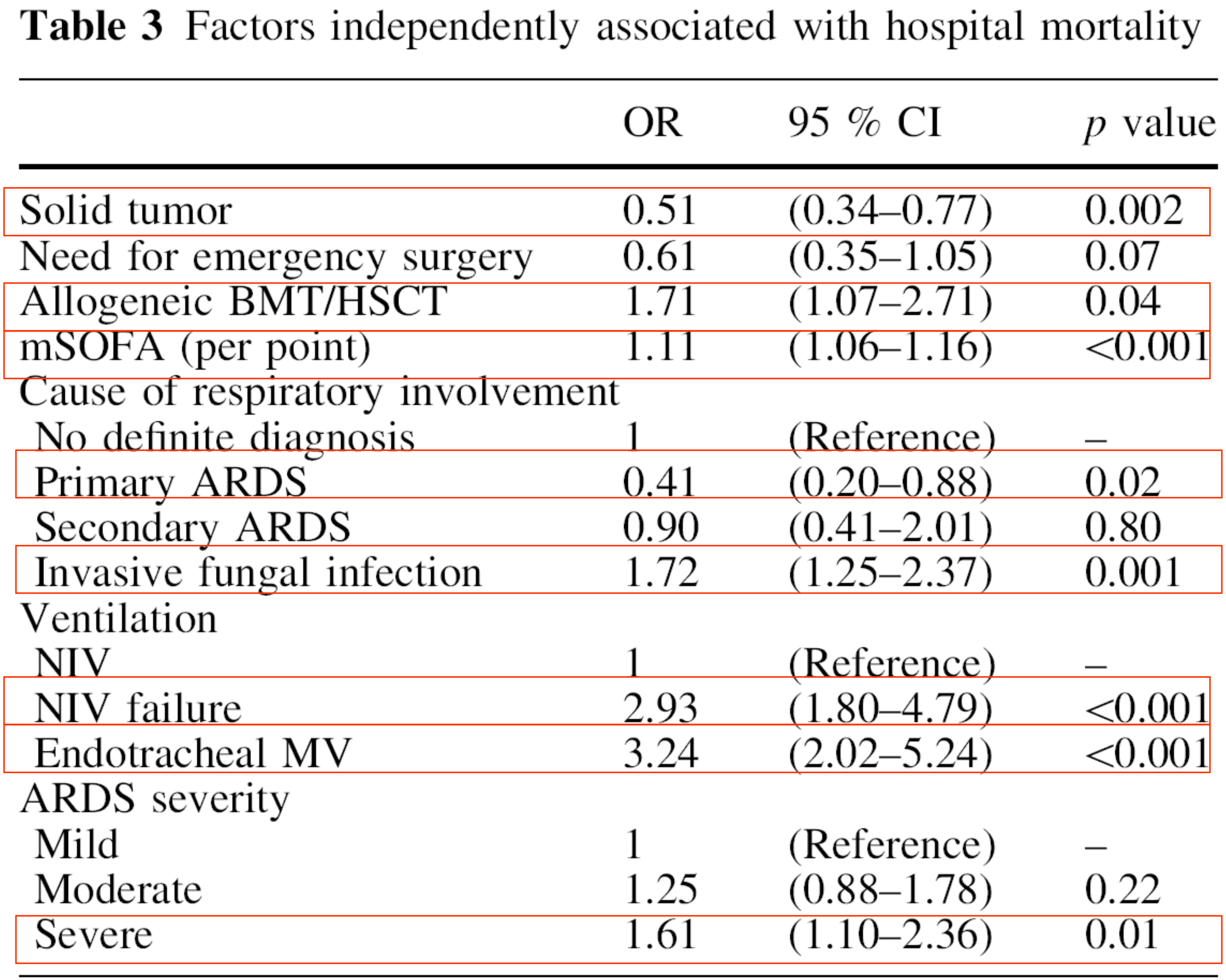


Table 3 Factors independently associated with hospital mortality

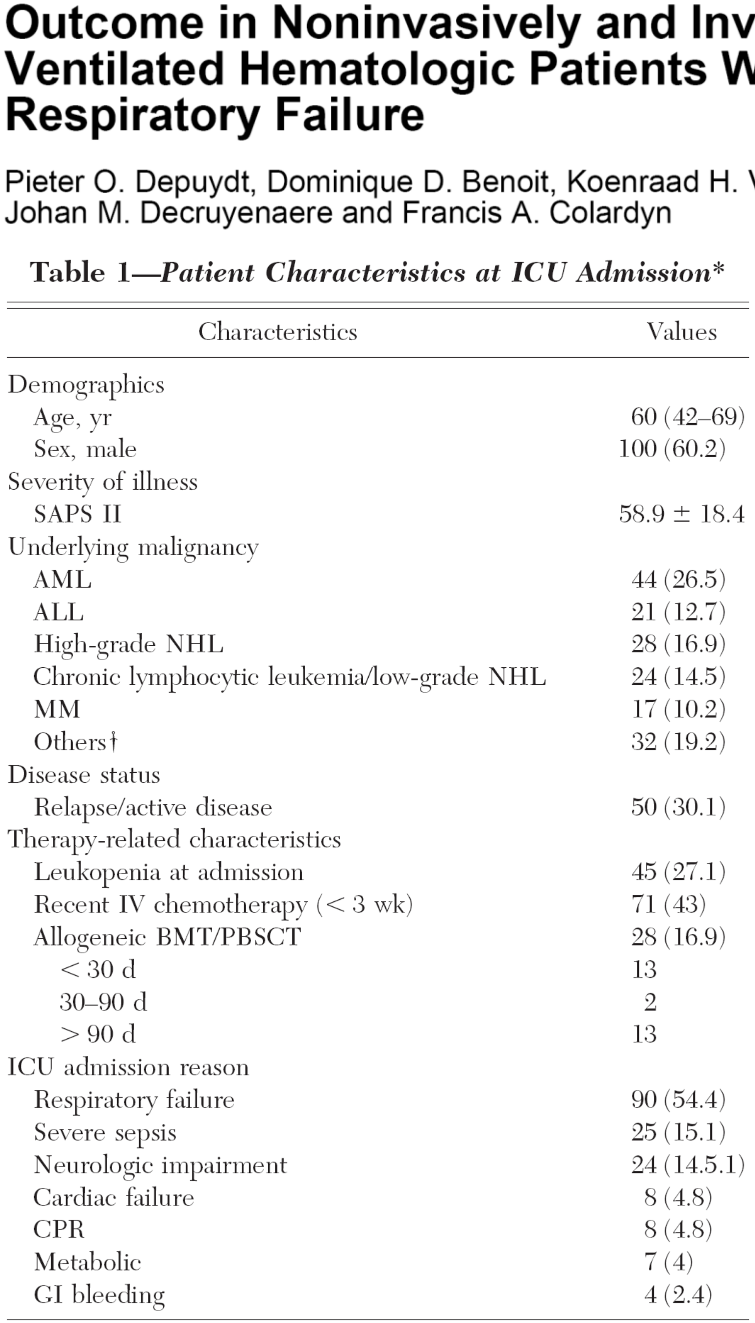
	OR	95 % CI	*p* value
Solid tumor	0.51	(0.34–0.77)	0.002
Need for emergency surgery	0.61	(0.35–1.05)	0.07
Allogeneic BMT/HSCT	1.71	(1.07–2.71)	0.04
mSOFA (per point)	1.11	(1.06–1.16)	<0.001
Cause of respiratory involvement			
No definite diagnosis	1	(Reference)	–
Primary ARDS	0.41	(0.20–0.88)	0.02
Secondary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

Intensive Care Med (2014) 40:1106–1114

Support ventilatoire

- VMI
- VNI
- Oxygène à haut débit
- ECMO

Ventilation mécanique invasive



Outcome in Noninvasively and Invasively Ventilated Hematologic Patients With Acute Respiratory Failure

Pieter O. Depuydt, Dominique D. Benoit, Koenraad H. Vandewoude,
Johan M. Decruyenaere and Francis A. Colardyn

Table 1—*Patient Characteristics at ICU Admission**

Characteristics	Values
Demographics	
Age, yr	60 (42–69)
Sex, male	100 (60.2)
Severity of illness	
SAPS II	58.9 ± 18.4
Underlying malignancy	
AML	44 (26.5)
ALL	21 (12.7)
High-grade NHL	28 (16.9)
Chronic lymphocytic leukemia/low-grade NHL	24 (14.5)
MM	17 (10.2)
Others†	32 (19.2)
Disease status	
Relapse/active disease	50 (30.1)
Therapy-related characteristics	
Leukopenia at admission	45 (27.1)
Recent IV chemotherapy (< 3 wk)	71 (43)
Allogeneic BMT/PBSCT	28 (16.9)
< 30 d	13
30–90 d	2
> 90 d	13
ICU admission reason	
Respiratory failure	90 (54.4)
Severe sepsis	25 (15.1)
Neurologic impairment	24 (14.5.1)
Cardiac failure	8 (4.8)
CPR	8 (4.8)
Metabolic	7 (4)
GI bleeding	4 (2.4)

Hospital mortality : 71%.

Chest 2004;126;1299-1306

Table 3—*Results From Stepwise Logistic Regression Procedure**

Variable	Parameter Estimate	OR	95% CI	p Value
Female sex	−1.01	0.36	0.16–0.82	0.014
Intubation < 24 h	−1.25	0.29	0.11–0.78	0.015
Bacteremia < 48 h	−1.52	0.22	0.08–0.61	0.003
AML	1.004	2.73	1.05–7.11	0.04
SAPS II	0.08	1.07	1.04–1.11	< 0.001

Outcome and predictors of mortality in patients requiring invasive mechanical ventilation due to acute respiratory failure while undergoing ambulatory chemotherapy for solid cancers

**So Young Park · So Yeon Lim · Sang-Won Um · Won-Jung Koh ·
Man Pyo Chung · Hojoong Kim · O Jung Kwon · Hye Kyeong Park ·
Seok Jin Kim · Young Hyuck Im · Myung-Ju Ahn · Gee Young Suh**

Table 1 Demographic and clinical characteristics of patients

Variables	Subjects (n=51)
Age, year	65 (25–87)
Sex(male)	38 (74.5 %)
Smoking[a]	
Smoker	28 (54.9 %)
Non-smoker	20 (39.2 %)
Comorbid conditions	
DM	4 (7.8 %)
HTN	7 (13.7 %)
Pulmonary TB	1 (2.0 %)
COPD	2 (3.9 %)
Primary site of solid cancer	
Lung	42 (82.3 %)
Colon	2 (3.9 %)
Stomach	5 (9.8 %)
Pancreas	1 (2 %)
Breast	1 (2 %)
Time from chemotherapy to admission in ICU (days)	7 (3–22)
ECOG PS	
0	2 (3.9 %)
1	8 (15.7 %)
2	38 (74.5 %)
3	3 (5.9 %)
SOFA	8 (5–14)
APACHE II	17 (7–32)
Treatment in ICU	
Vasopressor therapy	25 (49.0 %)
Renal replacement therapy	12 (23.5 %)
Tracheostomy	8 (15.7 %)
Duration of mechanical ventilation	4.5 (1–80)
Median ICU stay	7 (1–80)

ICU mortality 68%

Support Care Cancer (2013) 21:1647–1653

variables	Survivors	Non survivors	Unadjusted OR (CI) *P* value	Adjusted OR (CI)* *P* value
Age	62.4 (37–75)	59.5 (25–87)	1.051 (0.99–1.115) P=0.101	NA
Sex (male)	13 (34.2 %)	25 (65.8 %)	1.733 (0.405–7.418) P=0.458	NA
N	15 (7–31)	17.5 (12–32)	1.106 (0.996–1.228) P=0.06	NA
Smoking	9 (32 %)	19 (68 %)	1.000 (0.998–1.003) P= 0.942	0.897 (0.997–1.003) P=0.897
Primary site			0.897 (0.194–4.151) P=0.889	0.616 (0.116–3.268) P=0.570
Lung	13 (31 %)	29 (69 %)		
Others	3 (33 %)	6 (67 %)		
Time from chemotherapy (days)	7 (3–22)	10 (5–28)	1.028 (0.989–1.069) P=0.165	1.038 (0.995–1.082) P=0.084
Use of inotropics	10 (62.5 %)	15 (43 %)	2.22 (0.66–7.278) P=0.197	2.45 (0.072–8.943) P=0.174
Poor ECOG PS*	9 (22 %)	32 (78 %)	8.296 (1.776–38.75) P=0.007	6.554 (1.283–33.48) P=0.024
SOFA	7 (3–14)	10 (5–15)	1.179 (0.975–1.426) P=0.089	1.149 (0.939–1.407) P=0.177

100% mortalité si VMI « tardive »

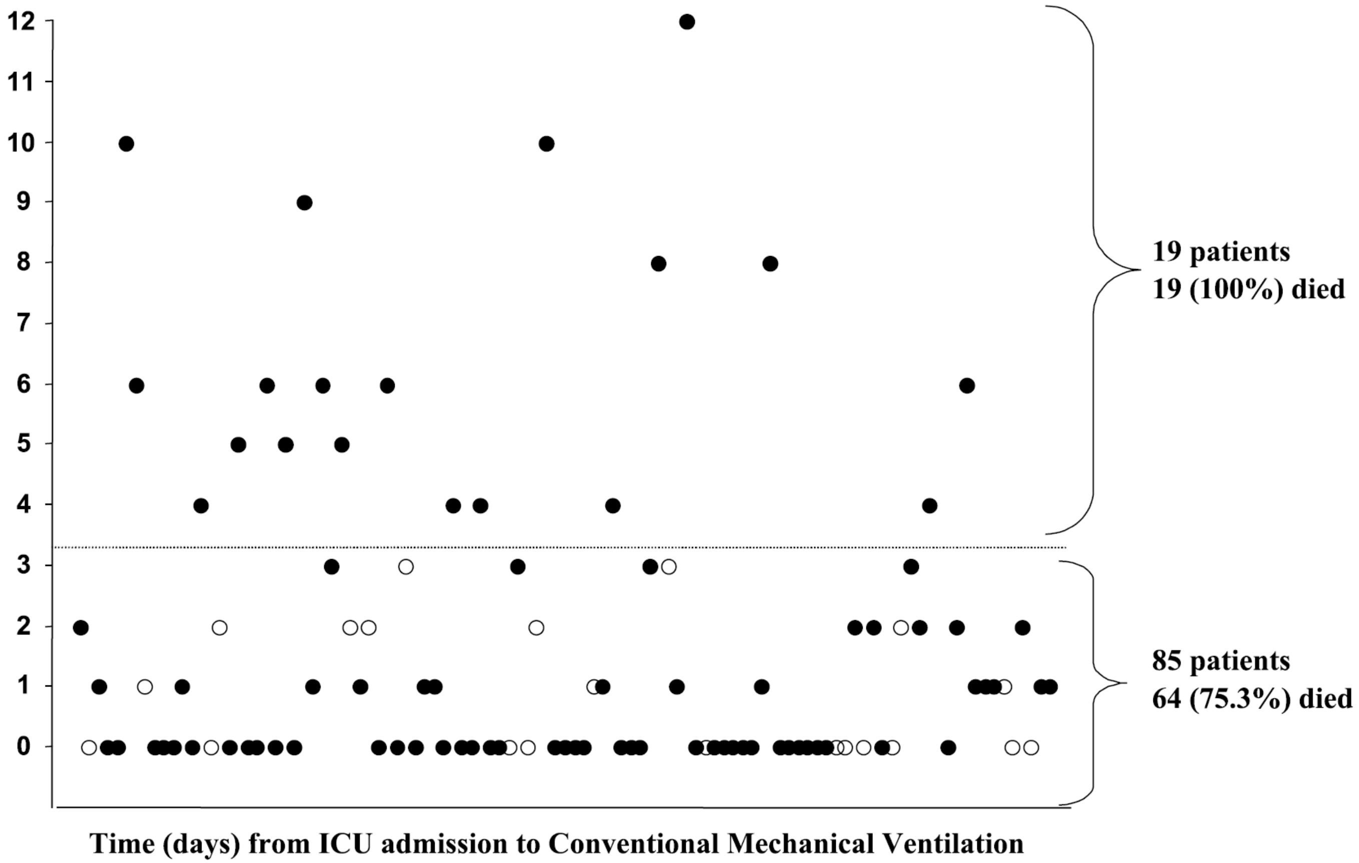


FIGURE 2. Time from ICU admission to mechanical ventilation (MV) in patients without cardiogenic pulmonary edema. Closed circles indicate patients who died; open circles indicate patients who survived. Of the 19 patients with a time to conventional MV longer than 3 days, 14 were on noninvasive MV. Ten patients with acute respiratory failure from cardiac pulmonary edema are not

Ventilation non invasive

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

Table 3. Multivariable analysis: Additive predictors of 30-day mortality

Variables	Odds ratio	95% CI	*p* Value
Noninvasive mechanical ventilation	0.343	0.16–0.73	<.0001
ICU admission between 1996 and 1998	0.24	0.12–0.50	<.0001
SAPS II score (per point)	1.04	1.02–1.06	<.0001

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(Crit Care Med 2001; 29:519–525)

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Ventilation non invasive

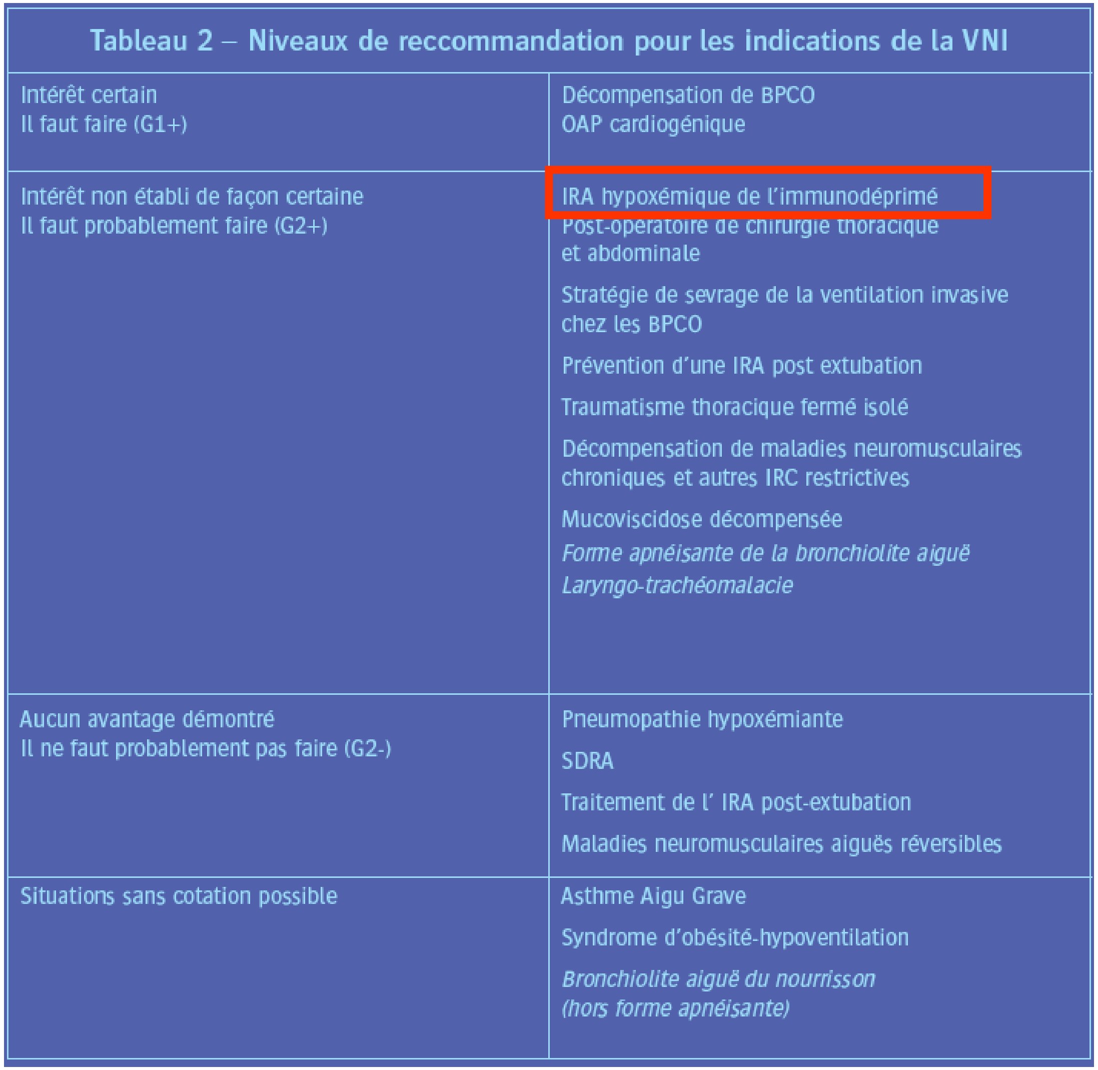

Tableau 2 – Niveaux de reccommandation pour les indications de la VNI

Intérêt certain Il faut faire (G1+)	Décompensation de BPCO OAP cardiogénique
Intérêt non établi de façon certaine Il faut probablement faire (G2+)	IRA hypoxémique de l'immunodéprimé Post-opératoire de chirurgie thoracique et abdominale Stratégie de sevrage de la ventilation invasive chez les BPCO Prévention d'une IRA post extubation Traumatisme thoracique fermé isolé Décompensation de maladies neuromusculaires chroniques et autres IRC restrictives Mucoviscidose décompensée *Forme apnéisante de la bronchiolite aiguë* *Laryngo-trachéomalacie*
Aucun avantage démontré Il ne faut probablement pas faire (G2-)	Pneumopathie hypoxémiante SDRA Traitement de l' IRA post-extubation Maladies neuromusculaires aiguës réversibles
Situations sans cotation possible	Asthme Aigu Grave Syndrome d'obésité-hypoventilation *Bronchiolite aiguë du nourrisson* *(hors forme apnéisante)*

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la SFAR, la SPLF et la SRLF

Ventilation Non Invasive
au cours de l'insuffisance respiratoire aiguë
(nouveau-né exclu)

Invasive mechanical ventilation in cancer patients. Prior non invasive ventilation is a poor prognostic factor

A.P. Meert, T. Berghmans, E. Markiewicz, M. Hardy, N. Nayer, M. Paesmans, J.P. Sculier

Table 1. Patient characteristics on admission

Characteristics	*Whole group*	*NIV followed by IMV*	*IMV alone*	*p-value*
Number of patients	164	41	123	
Median age, years (range)	57 (19-81)	49 (23-78)	59 (20-81)	0.008
Gender				0.86
Male, n	95	23	72	
Female, n	69	18	51	
Median SAPS II score (range)	53 (23-94)	56 (23-83)	47 (30-94)	0.002
Type of malignancy, n (%)				<0.001
Solid tumor	106 (64.6)	16 (39.0)	90 (73.2)	
Haematological malignancy	58 (35.4)	25 (61.0)	33 (26.8)	
Bone marrow /Peripheral blood stem cell transplantation, n (%)	37 (63.8)	19 (76.0)	18 (54.5)	<0.001
Cancer phase* (1,2 vs. 3,4), n (%)				0.006
Phase 1	5 (3.0)	1 (2.4)	4 (3.2)	
Phase 2	60 (36.6)	23 (56.1)	37 (30.1)	
Phase 3	89 (54.3)	17 (41.5)	72 (58.5)	
Phase 4	10 (6.1)	0 (0.0)	10 (8.1)	
Leukopenia at admission, n (%)	40 (24.4)	13 (31.7)	27 (21.9)	0.22
Median PaO_2/FiO_2 ratio (range)	215 (46-590)	183 (52-407)	230 (46-590)	0.02

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Journal of BUON **16:** 160-165, 2011

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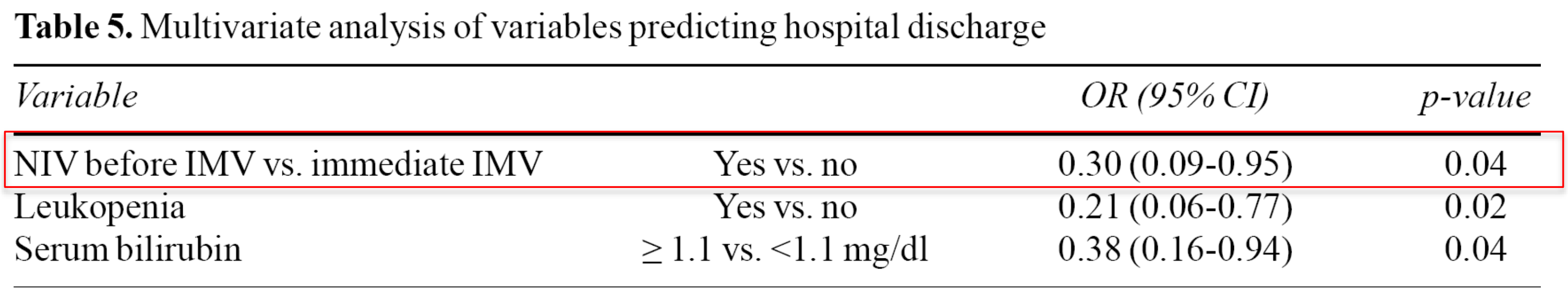


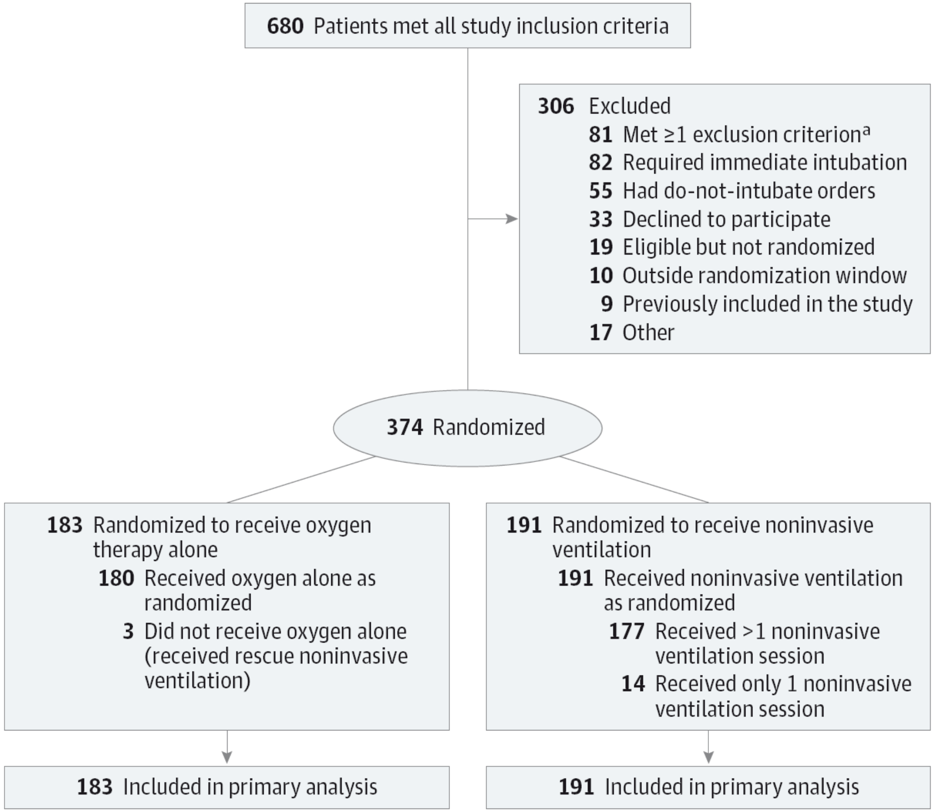
Table 5. Multivariate analysis of variables predicting hospital discharge

Variable		*OR (95% CI)*	*p-value*
NIV before IMV vs. immediate IMV	Yes vs. no	0.30 (0.09-0.95)	0.04
Leukopenia	Yes vs. no	0.21 (0.06-0.77)	0.02
Serum bilirubin	≥ 1.1 vs. <1.1 mg/dl	0.38 (0.16-0.94)	0.04

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

A Randomized Clinical Trial

Figure 1. Flow of Participants Through Study



680 Patients met all study inclusion criteria

306 Excluded
- **81** Met ≥1 exclusion criterion[a]
- **82** Required immediate intubation
- **55** Had do-not-intubate orders
- **33** Declined to participate
- **19** Eligible but not randomized
- **10** Outside randomization window
- **9** Previously included in the study
- **17** Other

374 Randomized

183 Randomized to receive oxygen therapy alone
- **180** Received oxygen alone as randomized
- **3** Did not receive oxygen alone (received rescue noninvasive ventilation)

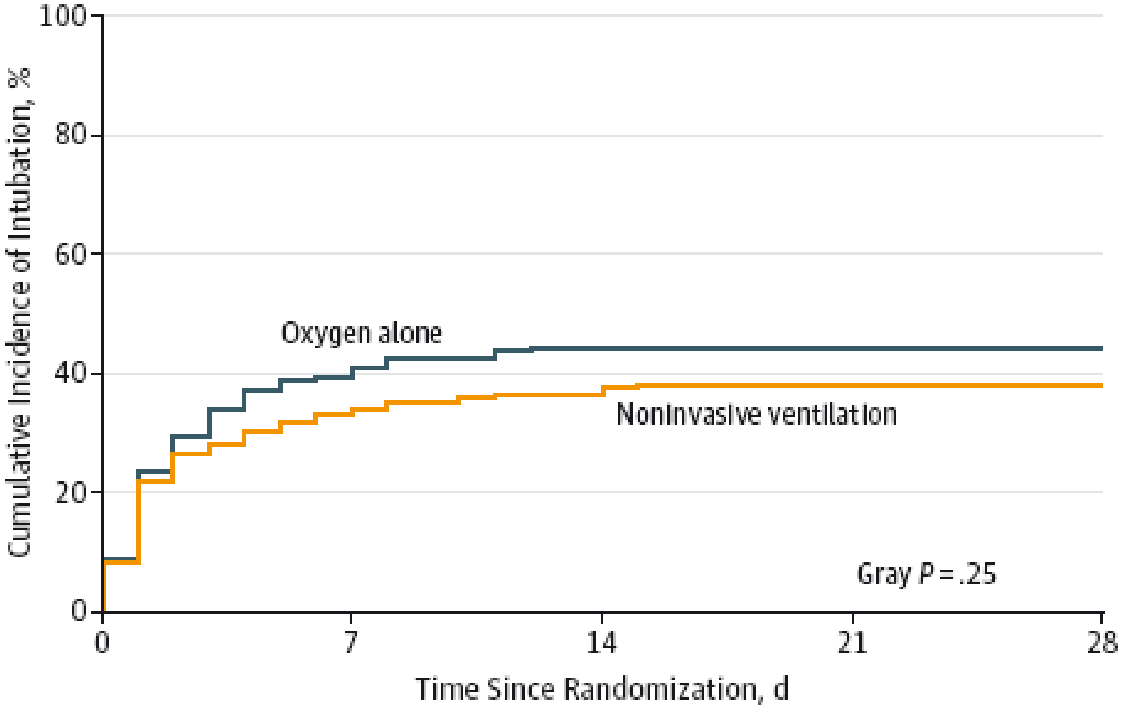
183 Included in primary analysis

191 Randomized to receive noninvasive ventilation
- **191** Received noninvasive ventilation as randomized
  - **177** Received >1 noninvasive ventilation session
  - **14** Received only 1 noninvasive ventilation session

191 Included in primary analysis

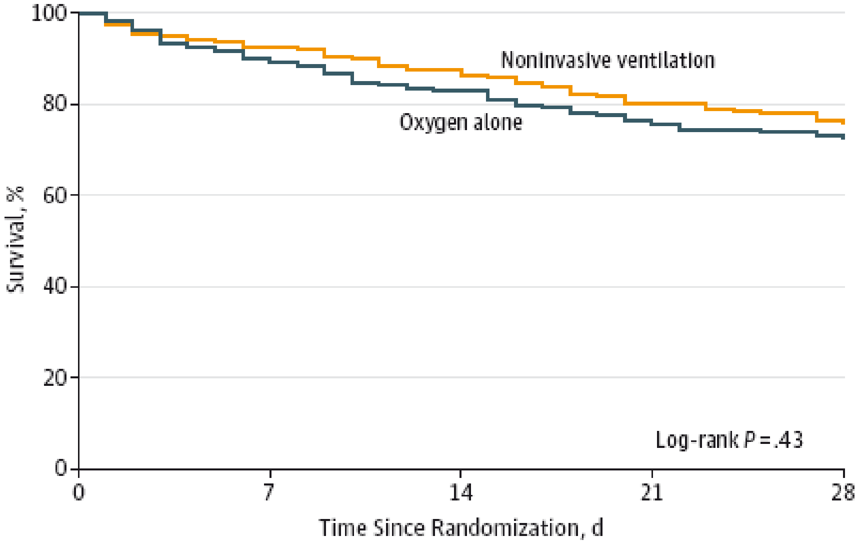
JAMA. doi:10.1001/jama.2015.12402

Figure 4. Cumulative Incidence of Intubation Throughout the 28 Days



No. at risk	0	7	14	21	28
Noninvasive ventilation	191	125	118	112	111
Oxygen alone	183	107	95	92	91

Figure 2. Probability of Survival at Day 28

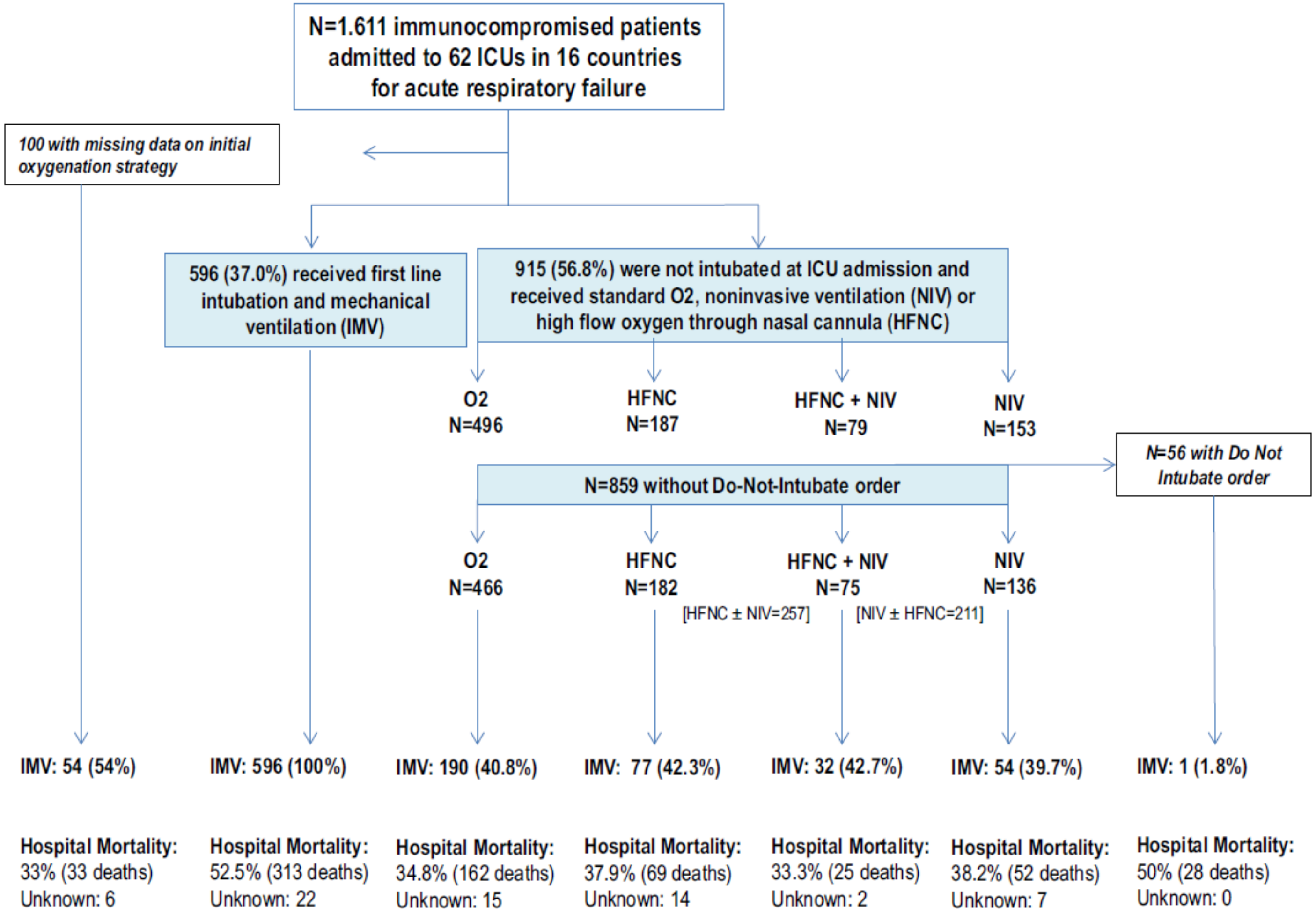


No. at risk	0	7	14	21	28
Noninvasive ventilation	191	177	167	153	146
Oxygen alone	183	165	152	140	134

Oxygène à haut débit

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

Elie Azoulay[1*], Peter Pickkers[2], Marcio Soares[3], Anders Perner[4], Jordi Rello[5], Philippe R. Bauer[6],



N=1.611 immunocompromised patients admitted to 62 ICUs in 16 countries for acute respiratory failure

100 with missing data on initial oxygenation strategy

596 (37.0%) received first line intubation and mechanical ventilation (IMV)

915 (56.8%) were not intubated at ICU admission and received standard O2, noninvasive ventilation (NIV) or high flow oxygen through nasal cannula (HFNC)

O2 N=496

HFNC N=187

HFNC + NIV N=79

NIV N=153

N=859 without Do-Not-Intubate order

N=56 with Do Not Intubate order

O2 N=466

HFNC N=182

HFNC + NIV N=75

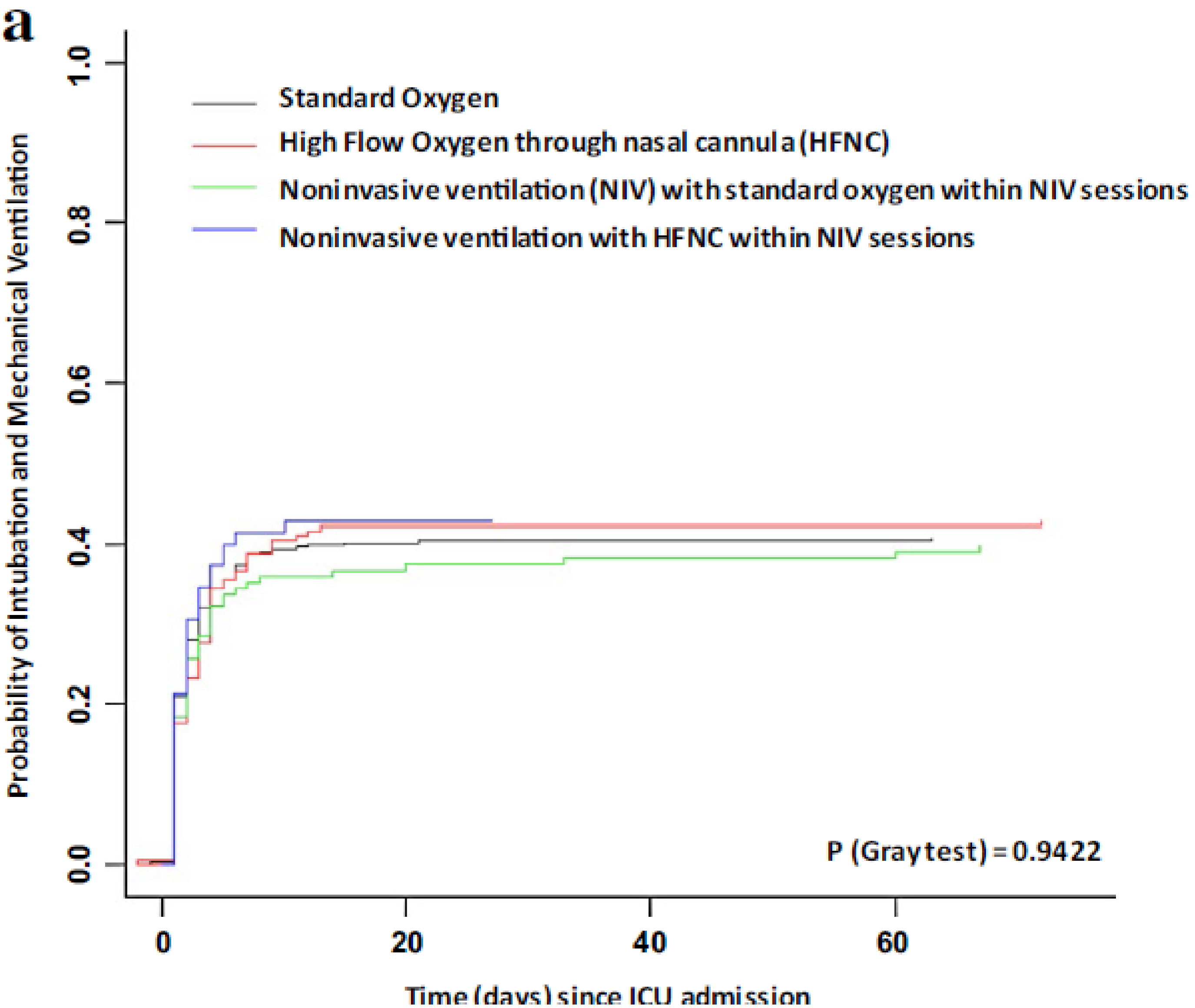
NIV N=136

[HFNC ± NIV=257]

[NIV ± HFNC=211]

IMV: 54 (54%)	**IMV: 596 (100%)**	**IMV: 190 (40.8%)**	**IMV: 77 (42.3%)**	**IMV: 32 (42.7%)**	**IMV: 54 (39.7%)**	**IMV: 1 (1.8%)**
Hospital Mortality: 33% (33 deaths) Unknown: 6	**Hospital Mortality:** 52.5% (313 deaths) Unknown: 22	**Hospital Mortality:** 34.8% (162 deaths) Unknown: 15	**Hospital Mortality:** 37.9% (69 deaths) Unknown: 14	**Hospital Mortality:** 33.3% (25 deaths) Unknown: 2	**Hospital Mortality:** 38.2% (52 deaths) Unknown: 7	**Hospital Mortality:** 50% (28 deaths) Unknown: 0

Intensive Care Med
DOI 10.1007/s00134-017-4947-1



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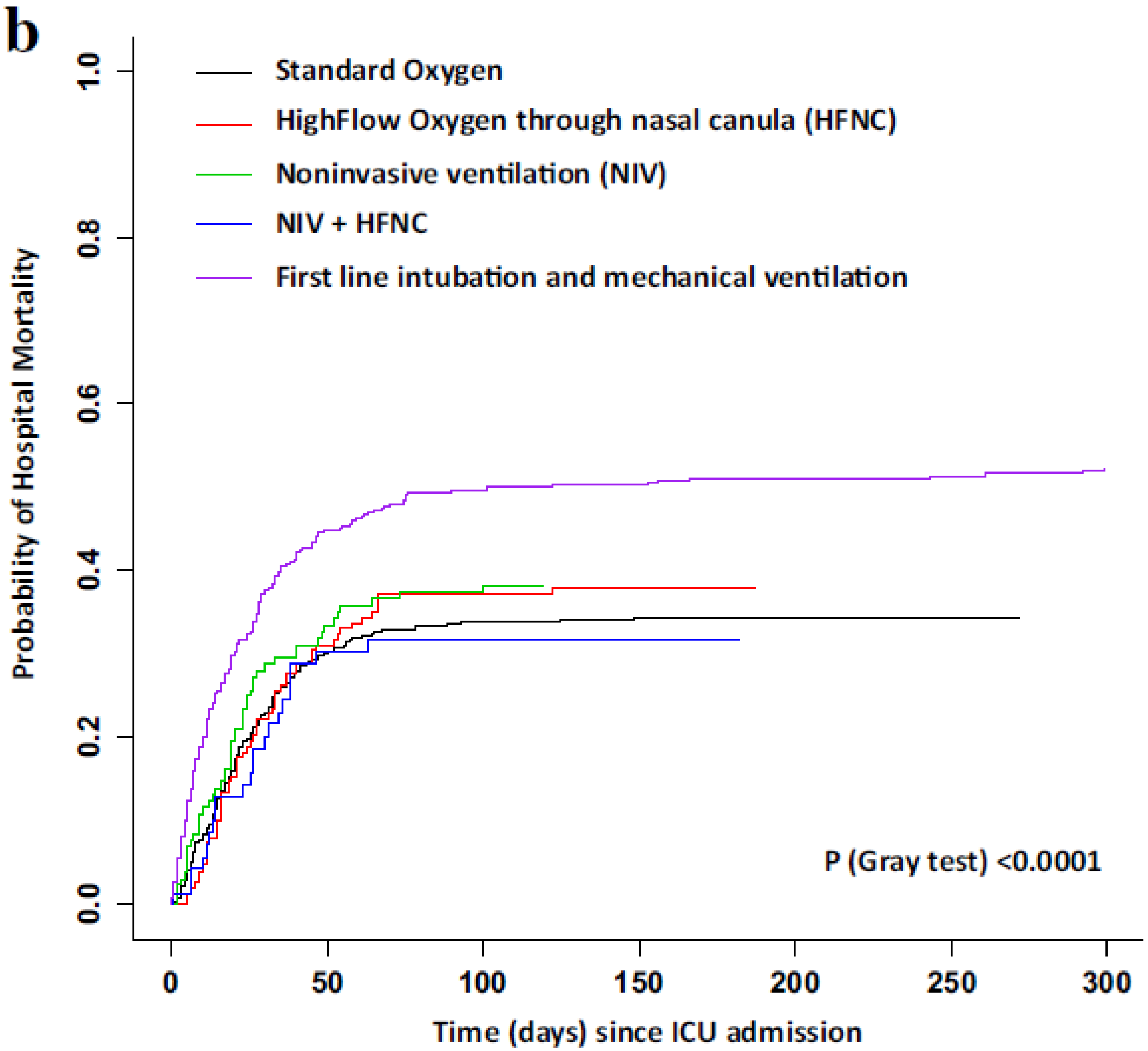
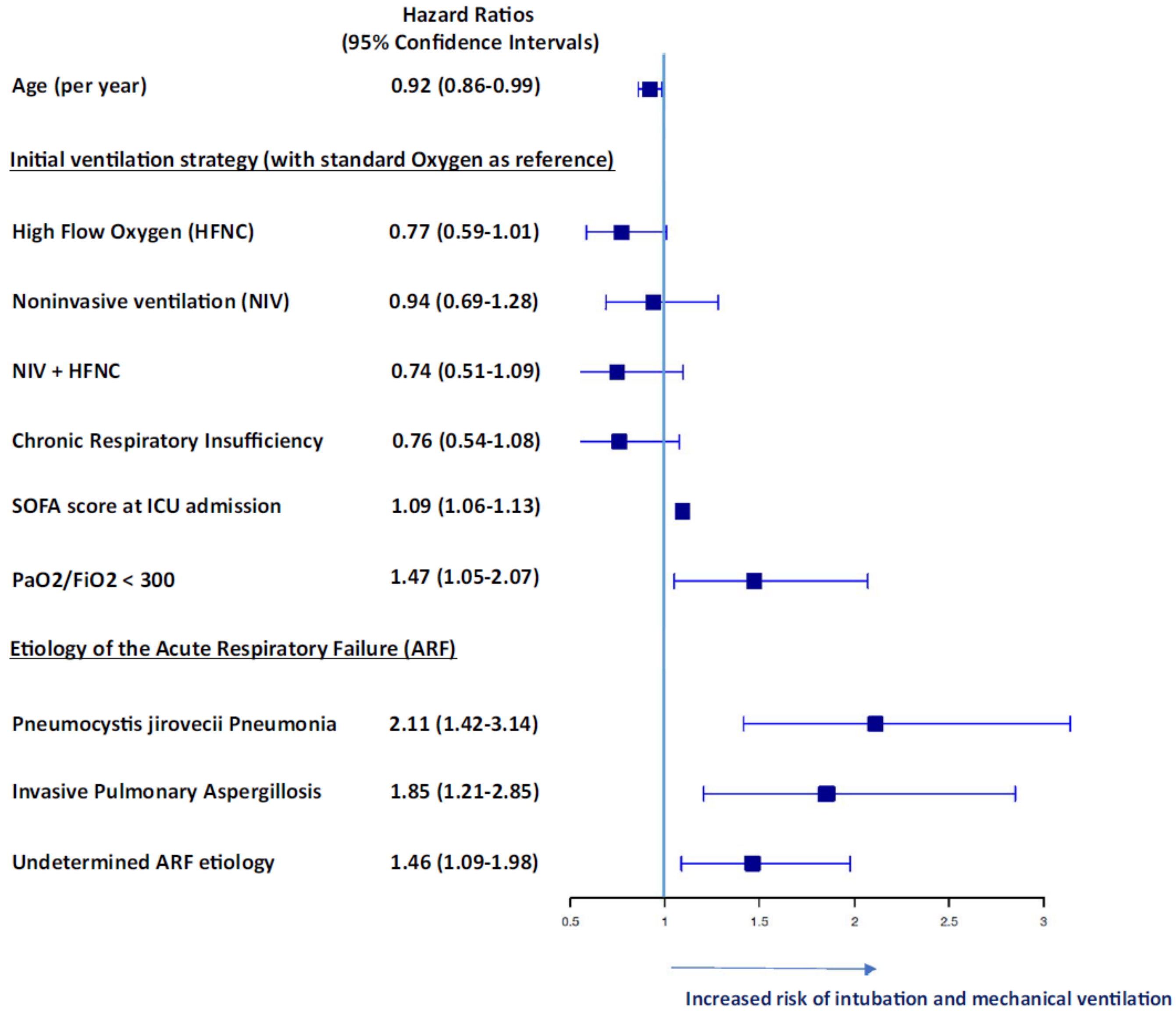

b
Standard Oxygen
HighFlow Oxygen through nasal canula (HFNC)
Noninvasive ventilation (NIV)
NIV + HFNC
First line intubation and mechanical ventilation
Probability of Hospital Mortality
0.0
0.2
0.4
0.6
0.8
1.0
0
50
100
150
200
250
300
Time (days) since ICU admission
P (Gray test) <0.0001



	Hazard Ratios (95% Confidence Intervals)
Age (per year)	0.92 (0.86-0.99)
Initial ventilation strategy (with standard Oxygen as reference)	
High Flow Oxygen (HFNC)	0.77 (0.59-1.01)
Noninvasive ventilation (NIV)	0.94 (0.69-1.28)
NIV + HFNC	0.74 (0.51-1.09)
Chronic Respiratory Insufficiency	0.76 (0.54-1.08)
SOFA score at ICU admission	1.09 (1.06-1.13)
PaO2/FiO2 < 300	1.47 (1.05-2.07)
Etiology of the Acute Respiratory Failure (ARF)	
Pneumocystis jirovecii Pneumonia	2.11 (1.42-3.14)
Invasive Pulmonary Aspergillosis	1.85 (1.21-2.85)
Undetermined ARF etiology	1.46 (1.09-1.98)

Fig. 3 Multivariate model of the cause-specific hazard of intubation. This analysis is restricted to the 915 patients not intubated on ICU admission. Plots report variables independently associated with the need for intubation in the final model, with their 95% confidence intervals

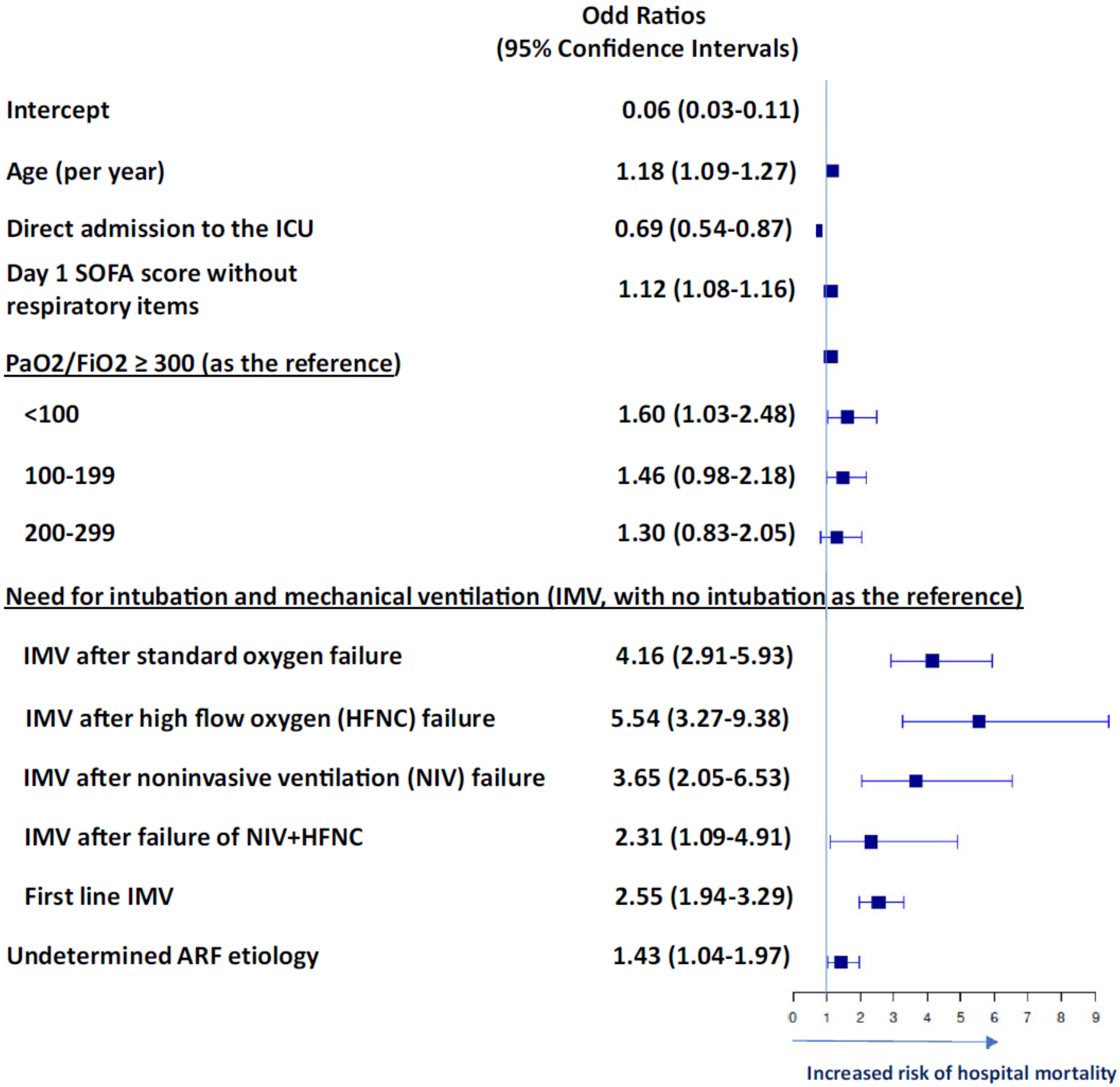
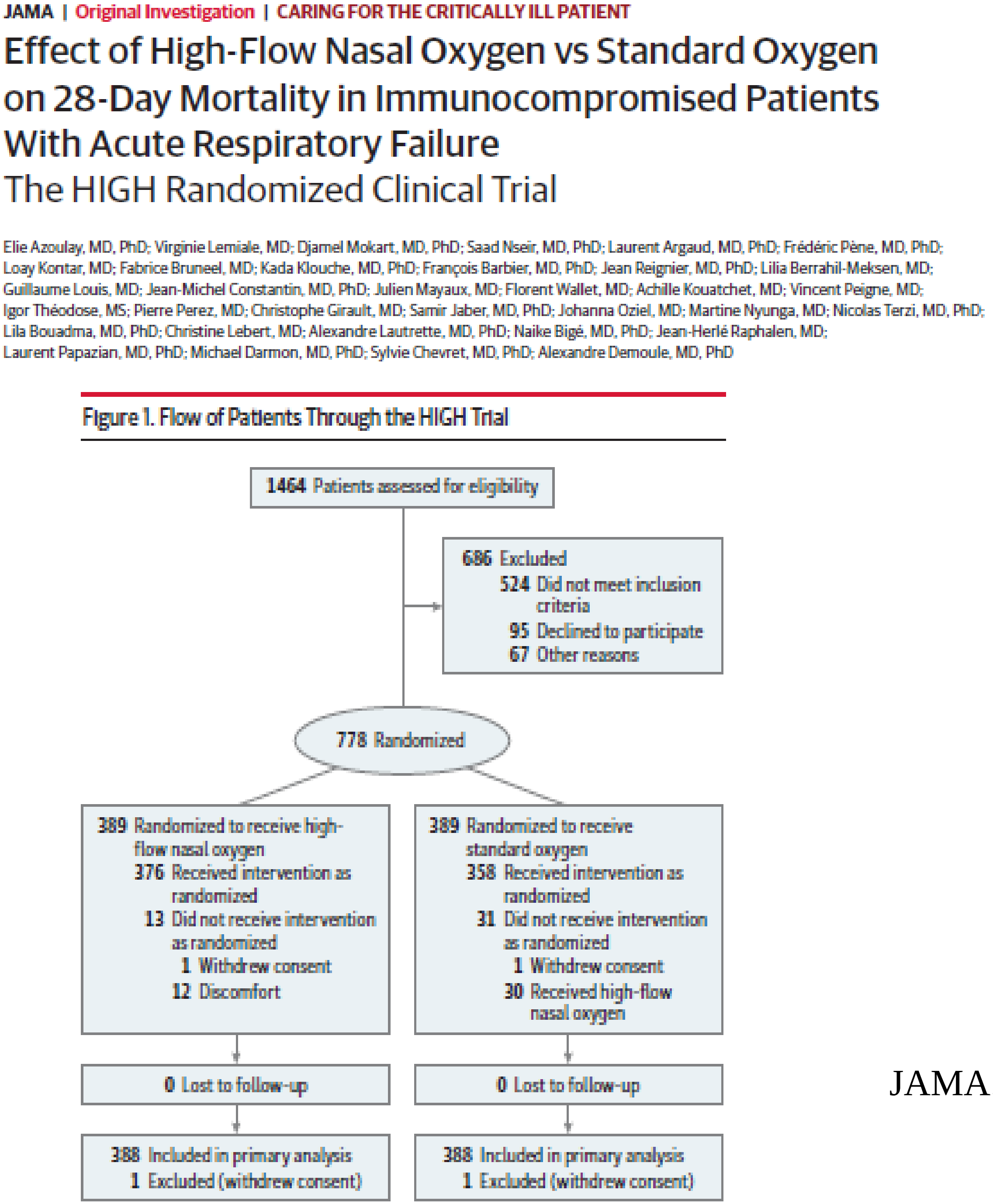


Fig. 4 Multivariate model of the prevalence of hospital death. This analysis is restricted to the 1545 patients with available status at hospital discharge. Plots report variables independently associated with hospital mortality in the final model, with their 95% confidence intervals



JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

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

The HIGH Randomized Clinical Trial

Elie Azoulay, MD, PhD; Virginie Lemiale, MD; Djamel Mokart, MD, PhD; Saad Nseir, MD, PhD; Laurent Argaud, MD, PhD; Frédéric Pène, MD, PhD; Loay Kontar, MD; Fabrice Bruneel, MD; Kada Klouche, MD, PhD; François Barbier, MD, PhD; Jean Reignier, MD, PhD; Lilia Berrahil-Meksen, MD; Guillaume Louis, MD; Jean-Michel Constantin, MD, PhD; Julien Mayaux, MD; Florent Wallet, MD; Achille Kouatchet, MD; Vincent Peigne, MD; Igor Théodose, MS; Pierre Perez, MD; Christophe Girault, MD; Samir Jaber, MD, PhD; Johanna Oziel, MD; Martine Nyunga, MD; Nicolas Terzi, MD, PhD; Lila Bouadma, MD, PhD; Christine Lebert, MD; Alexandre Lautrette, MD, PhD; Naike Bigé, MD, PhD; Jean-Herlé Raphalen, MD; Laurent Papazian, MD, PhD; Michael Darmon, MD, PhD; Sylvie Chevret, MD, PhD; Alexandre Demoule, MD, PhD

Figure 1. Flow of Patients Through the HIGH Trial

1464 Patients assessed for eligibility

686 Excluded
- **524** Did not meet inclusion criteria
- **95** Declined to participate
- **67** Other reasons

778 Randomized

389 Randomized to receive high-flow nasal oxygen
- **376** Received intervention as randomized
- **13** Did not receive intervention as randomized
  - **1** Withdrew consent
  - **12** Discomfort

0 Lost to follow-up

388 Included in primary analysis
- **1** Excluded (withdrew consent)

389 Randomized to receive standard oxygen
- **358** Received intervention as randomized
- **31** Did not receive intervention as randomized
  - **1** Withdrew consent
  - **30** Received high-flow nasal oxygen

0 Lost to follow-up

388 Included in primary analysis
- **1** Excluded (withdrew consent)

JAMA. 2018 Oct 24

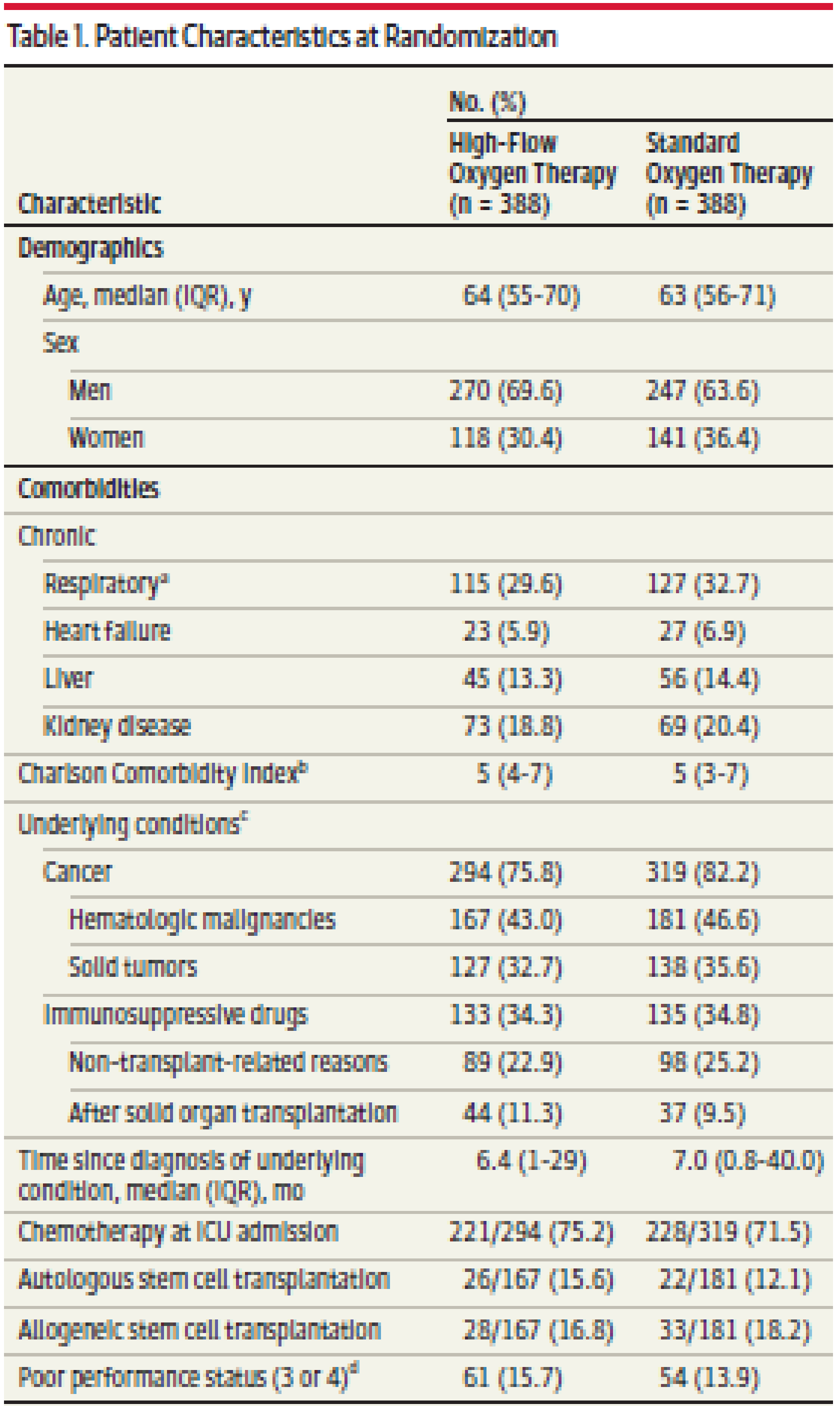


Table 1. Patient Characteristics at Randomization

	No. (%)	
Characteristic	High-Flow Oxygen Therapy (n = 388)	Standard Oxygen Therapy (n = 388)
Demographics		
Age, median (IQR), y	64 (55-70)	63 (56-71)
Sex		
Men	270 (69.6)	247 (63.6)
Women	118 (30.4)	141 (36.4)
Comorbidities		
Chronic		
Respiratory[a]	115 (29.6)	127 (32.7)
Heart failure	23 (5.9)	27 (6.9)
Liver	45 (13.3)	56 (14.4)
Kidney disease	73 (18.8)	69 (20.4)
Charlson Comorbidity Index[b]	5 (4-7)	5 (3-7)
Underlying conditions[c]		
Cancer	294 (75.8)	319 (82.2)
Hematologic malignancies	167 (43.0)	181 (46.6)
Solid tumors	127 (32.7)	138 (35.6)
Immunosuppressive drugs	133 (34.3)	135 (34.8)
Non-transplant-related reasons	89 (22.9)	98 (25.2)
After solid organ transplantation	44 (11.3)	37 (9.5)
Time since diagnosis of underlying condition, median (IQR), mo	6.4 (1-29)	7.0 (0.8-40.0)
Chemotherapy at ICU admission	221/294 (75.2)	228/319 (71.5)
Autologous stem cell transplantation	26/167 (15.6)	22/181 (12.1)
Allogeneic stem cell transplantation	28/167 (16.8)	33/181 (18.2)
Poor performance status (3 or 4)[d]	61 (15.7)	54 (13.9)

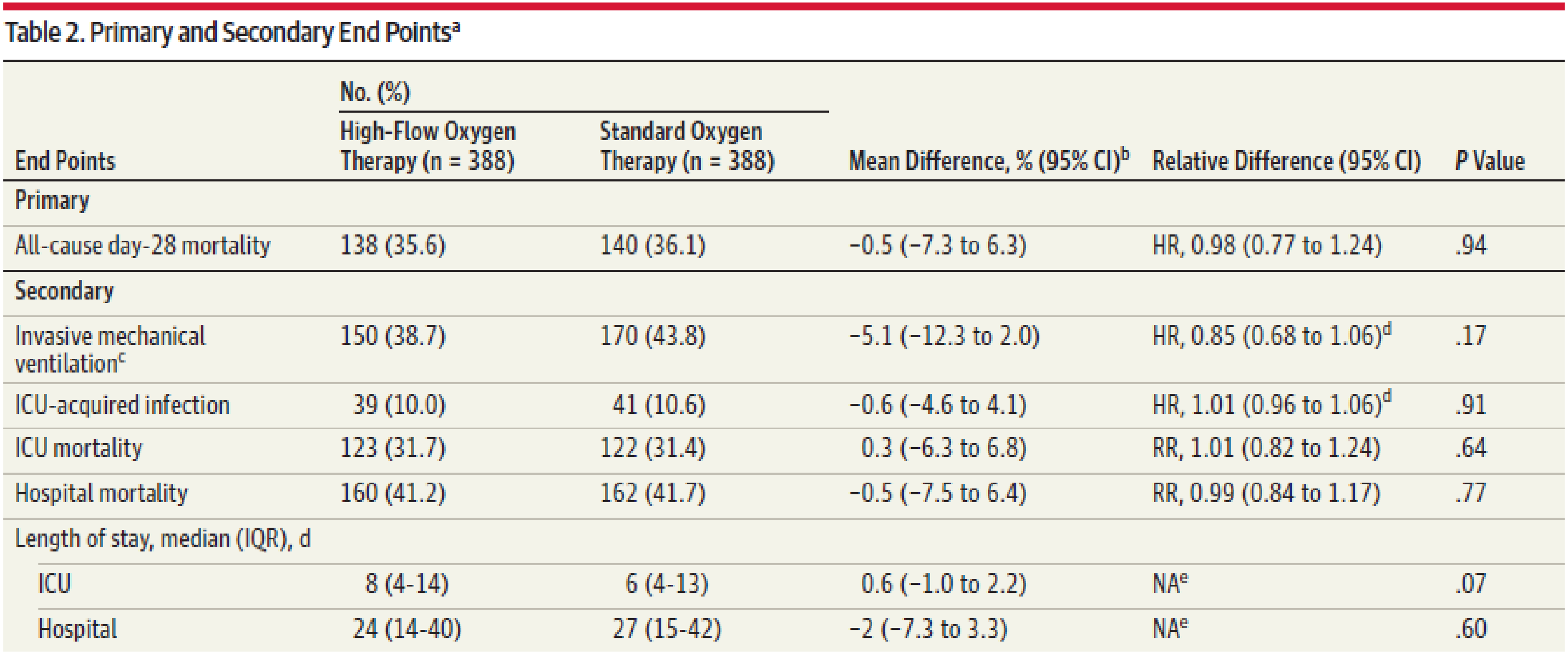
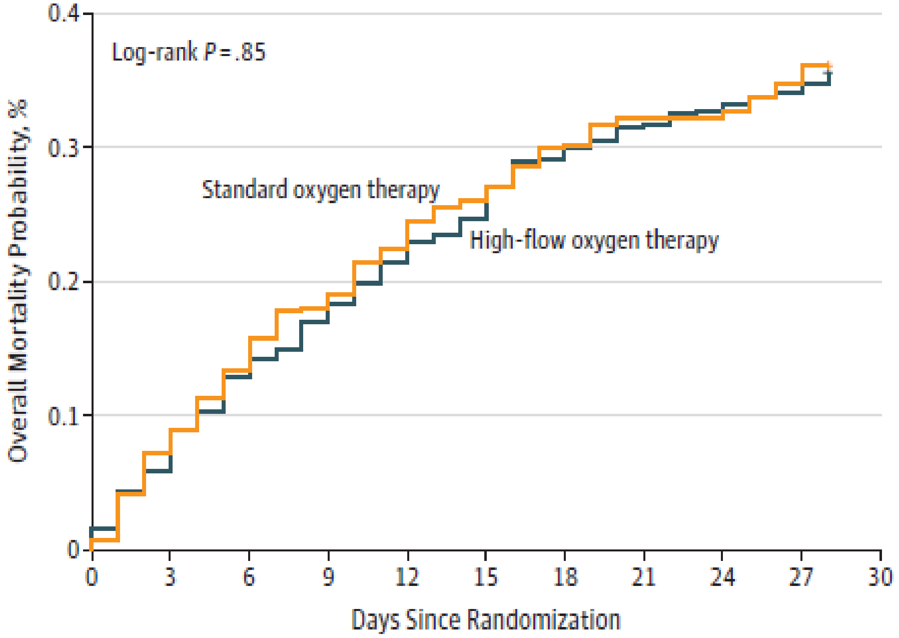


Table 2. Primary and Secondary End Points[a]

End Points	No. (%) High-Flow Oxygen Therapy (n = 388)	No. (%) Standard Oxygen Therapy (n = 388)	Mean Difference, % (95% CI)[b]	Relative Difference (95% CI)	*P* Value
Primary					
All-cause day-28 mortality	138 (35.6)	140 (36.1)	−0.5 (−7.3 to 6.3)	HR, 0.98 (0.77 to 1.24)	.94
Secondary					
Invasive mechanical ventilation[c]	150 (38.7)	170 (43.8)	−5.1 (−12.3 to 2.0)	HR, 0.85 (0.68 to 1.06)[d]	.17
ICU-acquired infection	39 (10.0)	41 (10.6)	−0.6 (−4.6 to 4.1)	HR, 1.01 (0.96 to 1.06)[d]	.91
ICU mortality	123 (31.7)	122 (31.4)	0.3 (−6.3 to 6.8)	RR, 1.01 (0.82 to 1.24)	.64
Hospital mortality	160 (41.2)	162 (41.7)	−0.5 (−7.5 to 6.4)	RR, 0.99 (0.84 to 1.17)	.77
Length of stay, median (IQR), d					
ICU	8 (4-14)	6 (4-13)	0.6 (−1.0 to 2.2)	NA[e]	.07
Hospital	24 (14-40)	27 (15-42)	−2 (−7.3 to 3.3)	NA[e]	.60

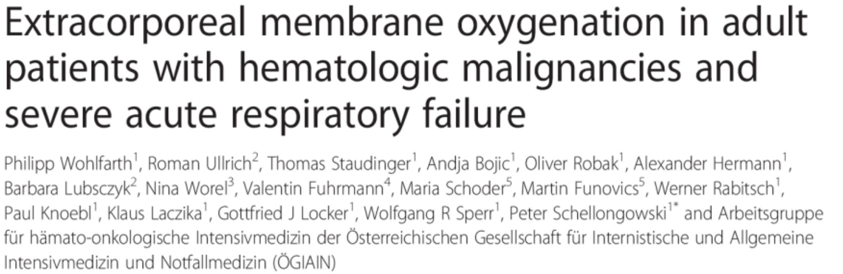
Figure 2. Probability of Day-28 Mortality in Immunocompromised Patients With Acute Respiratory Failure Receiving High-Flow Oxygen Therapy or Standard Oxygen Therapy



No. at risk											
High-flow oxygen therapy	388	365	338	322	305	292	275	266	261	256	0
Standard oxygen therapy	388	360	336	318	301	287	272	263	263	253	0

Median survival was not reached in either group.

ECMO



Extracorporeal membrane oxygenation in adult patients with hematologic malignancies and severe acute respiratory failure

Philipp Wohlfarth[1], Roman Ullrich[2], Thomas Staudinger[1], Andja Bojic[1], Oliver Robak[1], Alexander Hermann[1], Barbara Lubsczyk[2], Nina Worel[3], Valentin Fuhrmann[4], Maria Schoder[5], Martin Funovics[5], Werner Rabitsch[1], Paul Knoebl[1], Klaus Laczika[1], Gottfried J Locker[1], Wolfgang R Sperr[1], Peter Schellongowski[1*] and Arbeitsgruppe für hämato-onkologische Intensivmedizin der Österreichischen Gesellschaft für Internistische und Allgemeine Intensivmedizin und Notfallmedizin (ÖGIAIN)

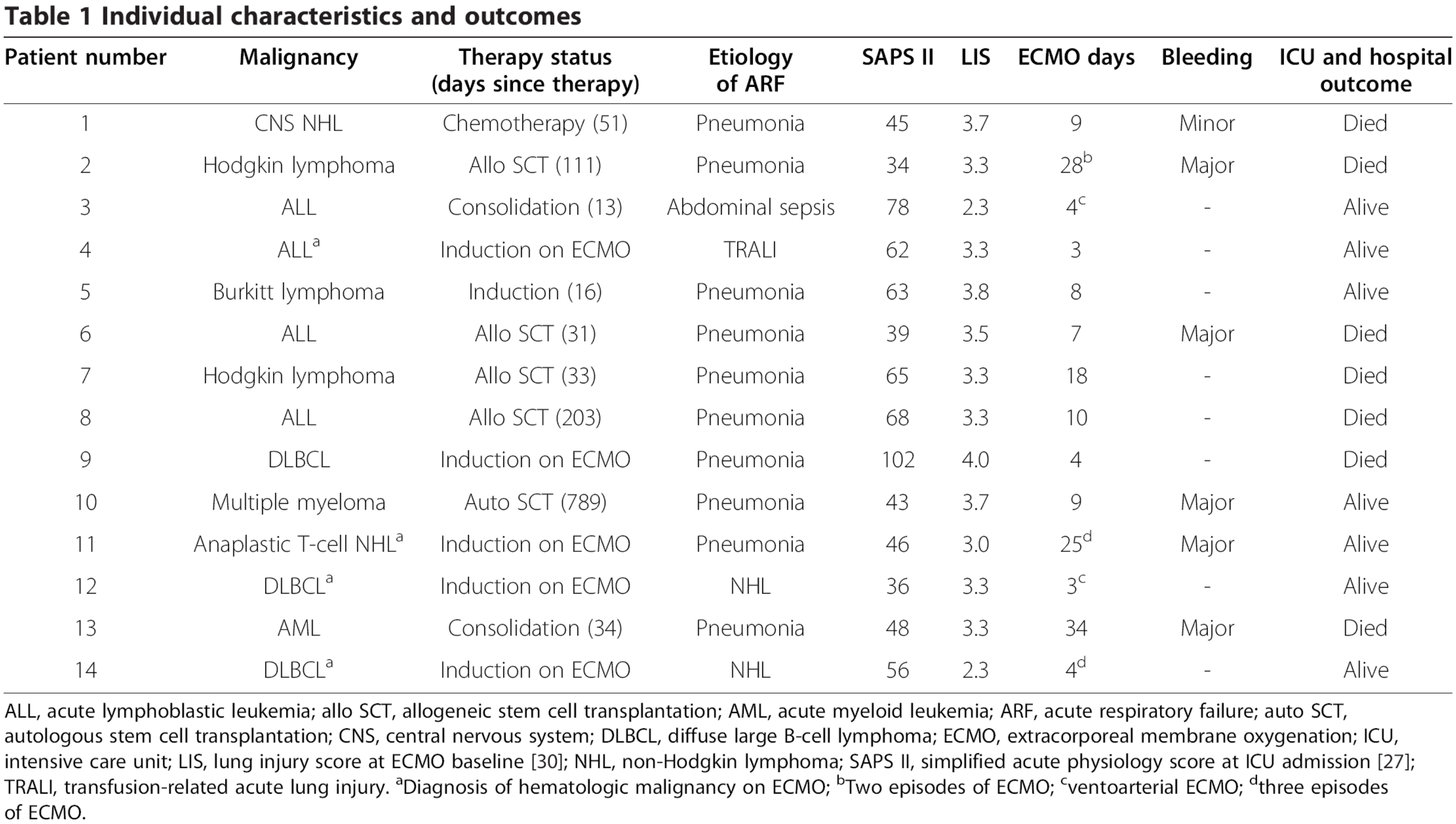


Table 1 Individual characteristics and outcomes

Patient number	Malignancy	Therapy status (days since therapy)	Etiology of ARF	SAPS II	LIS	ECMO days	Bleeding	ICU and hospital outcome
1	CNS NHL	Chemotherapy (51)	Pneumonia	45	3.7	9	Minor	Died
2	Hodgkin lymphoma	Allo SCT (111)	Pneumonia	34	3.3	28[b]	Major	Died
3	ALL	Consolidation (13)	Abdominal sepsis	78	2.3	4[c]	-	Alive
4	ALL[a]	Induction on ECMO	TRALI	62	3.3	3	-	Alive
5	Burkitt lymphoma	Induction (16)	Pneumonia	63	3.8	8	-	Alive
6	ALL	Allo SCT (31)	Pneumonia	39	3.5	7	Major	Died
7	Hodgkin lymphoma	Allo SCT (33)	Pneumonia	65	3.3	18	-	Died
8	ALL	Allo SCT (203)	Pneumonia	68	3.3	10	-	Died
9	DLBCL	Induction on ECMO	Pneumonia	102	4.0	4	-	Died
10	Multiple myeloma	Auto SCT (789)	Pneumonia	43	3.7	9	Major	Alive
11	Anaplastic T-cell NHL[a]	Induction on ECMO	Pneumonia	46	3.0	25[d]	Major	Alive
12	DLBCL[a]	Induction on ECMO	NHL	36	3.3	3[c]	-	Alive
13	AML	Consolidation (34)	Pneumonia	48	3.3	34	Major	Died
14	DLBCL[a]	Induction on ECMO	NHL	56	2.3	4[d]	-	Alive

ALL, acute lymphoblastic leukemia; allo SCT, allogeneic stem cell transplantation; AML, acute myeloid leukemia; ARF, acute respiratory failure; auto SCT, autologous stem cell transplantation; CNS, central nervous system; DLBCL, diffuse large B-cell lymphoma; ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit; LIS, lung injury score at ECMO baseline [30]; NHL, non-Hodgkin lymphoma; SAPS II, simplified acute physiology score at ICU admission [27]; TRALI, transfusion-related acute lung injury. [a]Diagnosis of hematologic malignancy on ECMO; [b]Two episodes of ECMO; [c]ventoarterial ECMO; [d]three episodes of ECMO.

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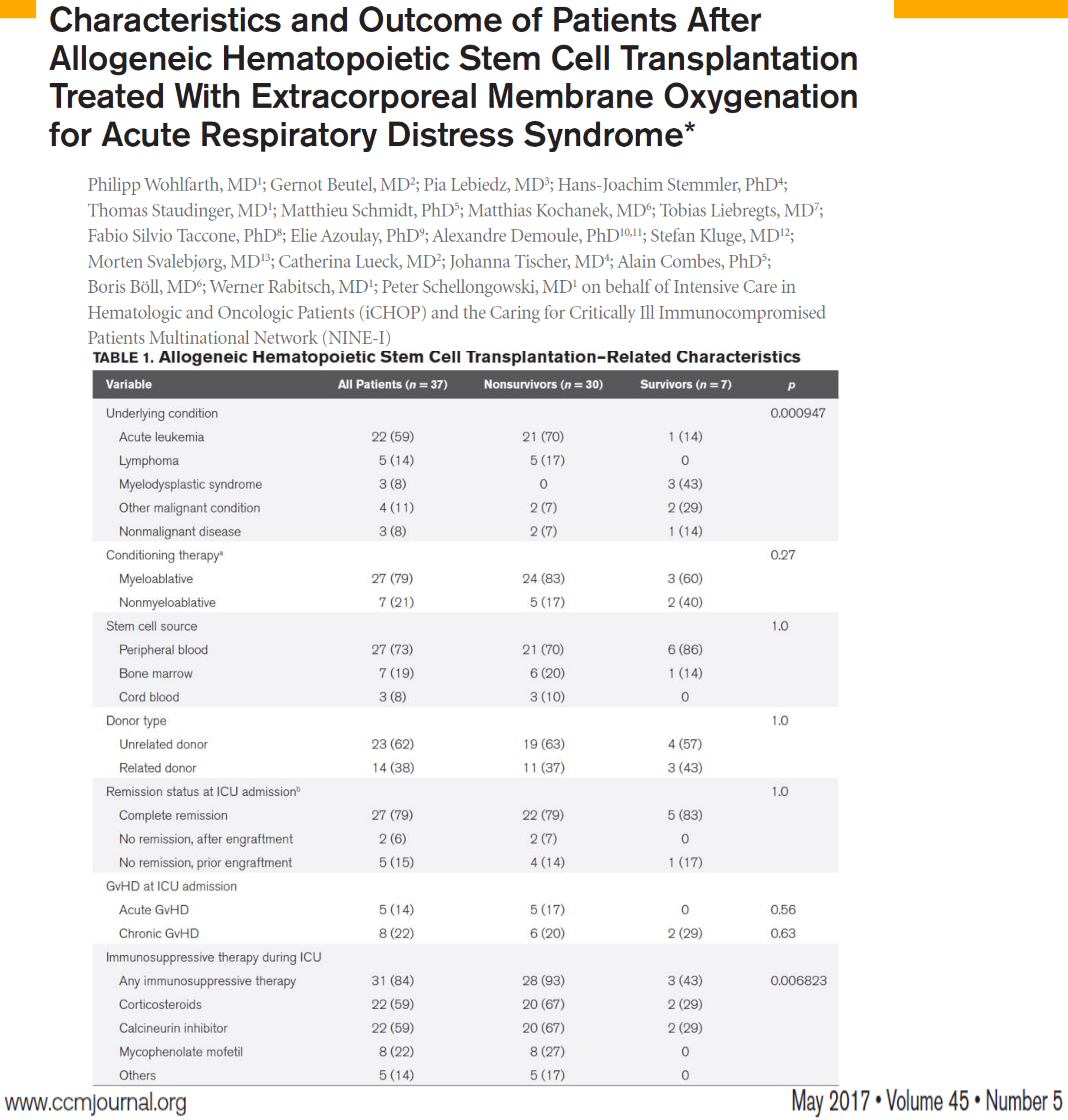

Characteristics and Outcome of Patients After Allogeneic Hematopoietic Stem Cell Transplantation Treated With Extracorporeal Membrane Oxygenation for Acute Respiratory Distress Syndrome*

Philipp Wohlfarth, MD[1]; Gernot Beutel, MD[2]; Pia Lebiedz, MD[3]; Hans-Joachim Stemmler, PhD[4]; Thomas Staudinger, MD[1]; Matthieu Schmidt, PhD[5]; Matthias Kochanek, MD[6]; Tobias Liebregts, MD[7]; Fabio Silvio Taccone, PhD[8]; Elie Azoulay, PhD[9]; Alexandre Demoule, PhD[10,11]; Stefan Kluge, MD[12]; Morten Svalebjørg, MD[13]; Catherina Lueck, MD[2]; Johanna Tischer, MD[4]; Alain Combes, PhD[5]; Boris Böll, MD[6]; Werner Rabitsch, MD[1]; Peter Schellongowski, MD[1] on behalf of Intensive Care in Hematologic and Oncologic Patients (iCHOP) and the Caring for Critically Ill Immunocompromised Patients Multinational Network (NINE-I)

TABLE 1. Allogeneic Hematopoietic Stem Cell Transplantation–Related Characteristics

Variable	All Patients (*n* = 37)	Nonsurvivors (*n* = 30)	Survivors (*n* = 7)	*p*
Underlying condition				0.000947
Acute leukemia	22 (59)	21 (70)	1 (14)	
Lymphoma	5 (14)	5 (17)	0	
Myelodysplastic syndrome	3 (8)	0	3 (43)	
Other malignant condition	4 (11)	2 (7)	2 (29)	
Nonmalignant disease	3 (8)	2 (7)	1 (14)	
Conditioning therapy[a]				0.27
Myeloablative	27 (79)	24 (83)	3 (60)	
Nonmyeloablative	7 (21)	5 (17)	2 (40)	
Stem cell source				1.0
Peripheral blood	27 (73)	21 (70)	6 (86)	
Bone marrow	7 (19)	6 (20)	1 (14)	
Cord blood	3 (8)	3 (10)	0	
Donor type				1.0
Unrelated donor	23 (62)	19 (63)	4 (57)	
Related donor	14 (38)	11 (37)	3 (43)	
Remission status at ICU admission[b]				1.0
Complete remission	27 (79)	22 (79)	5 (83)	
No remission, after engraftment	2 (6)	2 (7)	0	
No remission, prior engraftment	5 (15)	4 (14)	1 (17)	
GvHD at ICU admission				
Acute GvHD	5 (14)	5 (17)	0	0.56
Chronic GvHD	8 (22)	6 (20)	2 (29)	0.63
Immunosuppressive therapy during ICU				
Any immunosuppressive therapy	31 (84)	28 (93)	3 (43)	0.006823
Corticosteroids	22 (59)	20 (67)	2 (29)	
Calcineurin inhibitor	22 (59)	20 (67)	2 (29)	
Mycophenolate mofetil	8 (22)	8 (27)	0	
Others	5 (14)	5 (17)	0	

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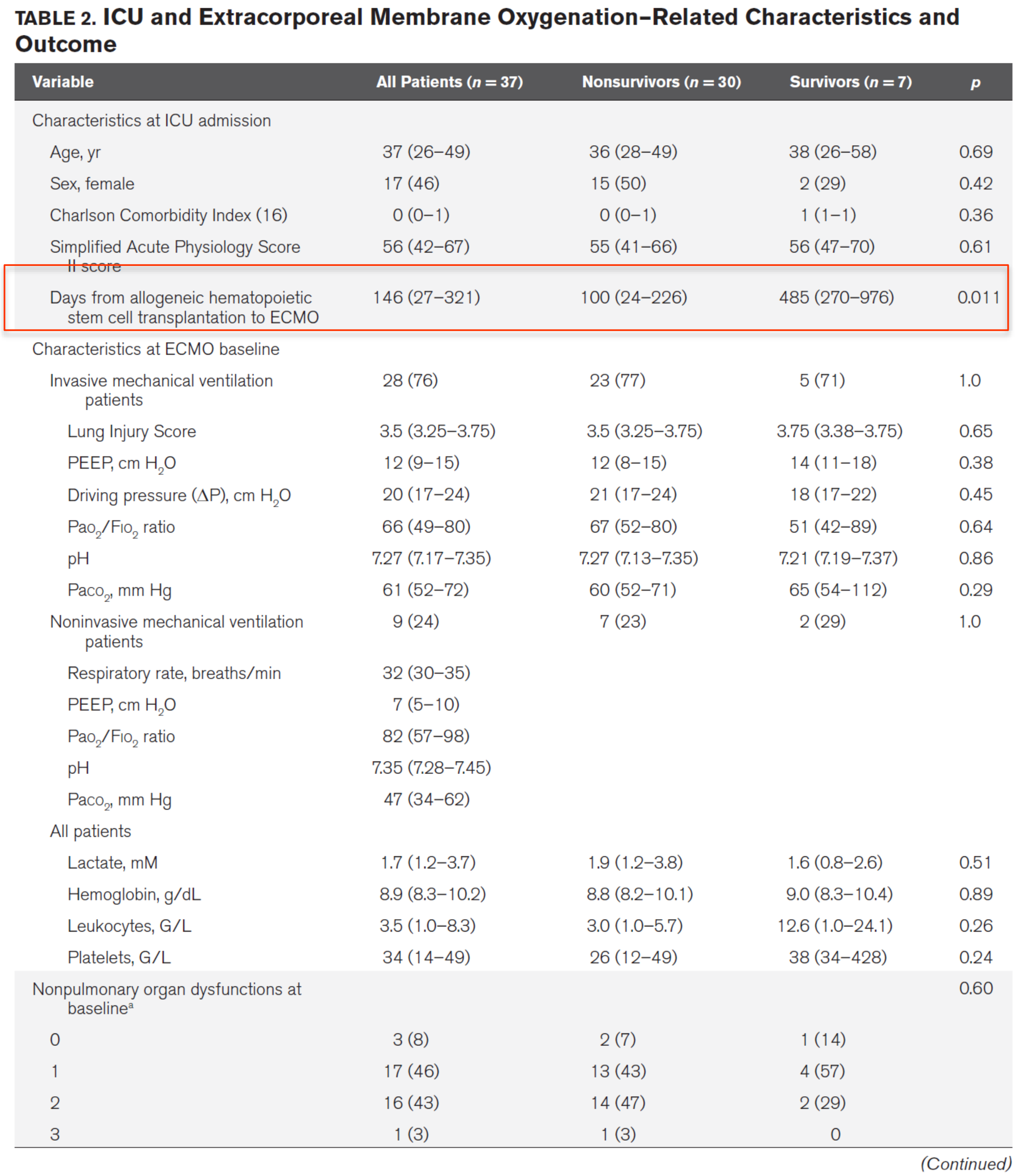

TABLE 2. **ICU and Extracorporeal Membrane Oxygenation–Related Characteristics and Outcome**

Variable	All Patients ($n = 37$)	Nonsurvivors ($n = 30$)	Survivors ($n = 7$)	p
Characteristics at ICU admission				
Age, yr	37 (26–49)	36 (28–49)	38 (26–58)	0.69
Sex, female	17 (46)	15 (50)	2 (29)	0.42
Charlson Comorbidity Index (16)	0 (0–1)	0 (0–1)	1 (1–1)	0.36
Simplified Acute Physiology Score II score	56 (42–67)	55 (41–66)	56 (47–70)	0.61
Days from allogeneic hematopoietic stem cell transplantation to ECMO	146 (27–321)	100 (24–226)	485 (270–976)	0.011
Characteristics at ECMO baseline				
Invasive mechanical ventilation patients	28 (76)	23 (77)	5 (71)	1.0
Lung Injury Score	3.5 (3.25–3.75)	3.5 (3.25–3.75)	3.75 (3.38–3.75)	0.65
PEEP, cm H_2O	12 (9–15)	12 (8–15)	14 (11–18)	0.38
Driving pressure (ΔP), cm H_2O	20 (17–24)	21 (17–24)	18 (17–22)	0.45
Pao_2/Fio_2 ratio	66 (49–80)	67 (52–80)	51 (42–89)	0.64
pH	7.27 (7.17–7.35)	7.27 (7.13–7.35)	7.21 (7.19–7.37)	0.86
$Paco_2$, mm Hg	61 (52–72)	60 (52–71)	65 (54–112)	0.29
Noninvasive mechanical ventilation patients	9 (24)	7 (23)	2 (29)	1.0
Respiratory rate, breaths/min	32 (30–35)			
PEEP, cm H_2O	7 (5–10)			
Pao_2/Fio_2 ratio	82 (57–98)			
pH	7.35 (7.28–7.45)			
$Paco_2$, mm Hg	47 (34–62)			
All patients				
Lactate, mM	1.7 (1.2–3.7)	1.9 (1.2–3.8)	1.6 (0.8–2.6)	0.51
Hemoglobin, g/dL	8.9 (8.3–10.2)	8.8 (8.2–10.1)	9.0 (8.3–10.4)	0.89
Leukocytes, G/L	3.5 (1.0–8.3)	3.0 (1.0–5.7)	12.6 (1.0–24.1)	0.26
Platelets, G/L	34 (14–49)	26 (12–49)	38 (34–428)	0.24
Nonpulmonary organ dysfunctions at baseline[a]				0.60
0	3 (8)	2 (7)	1 (14)	
1	17 (46)	13 (43)	4 (57)	
2	16 (43)	14 (47)	2 (29)	
3	1 (3)	1 (3)	0	

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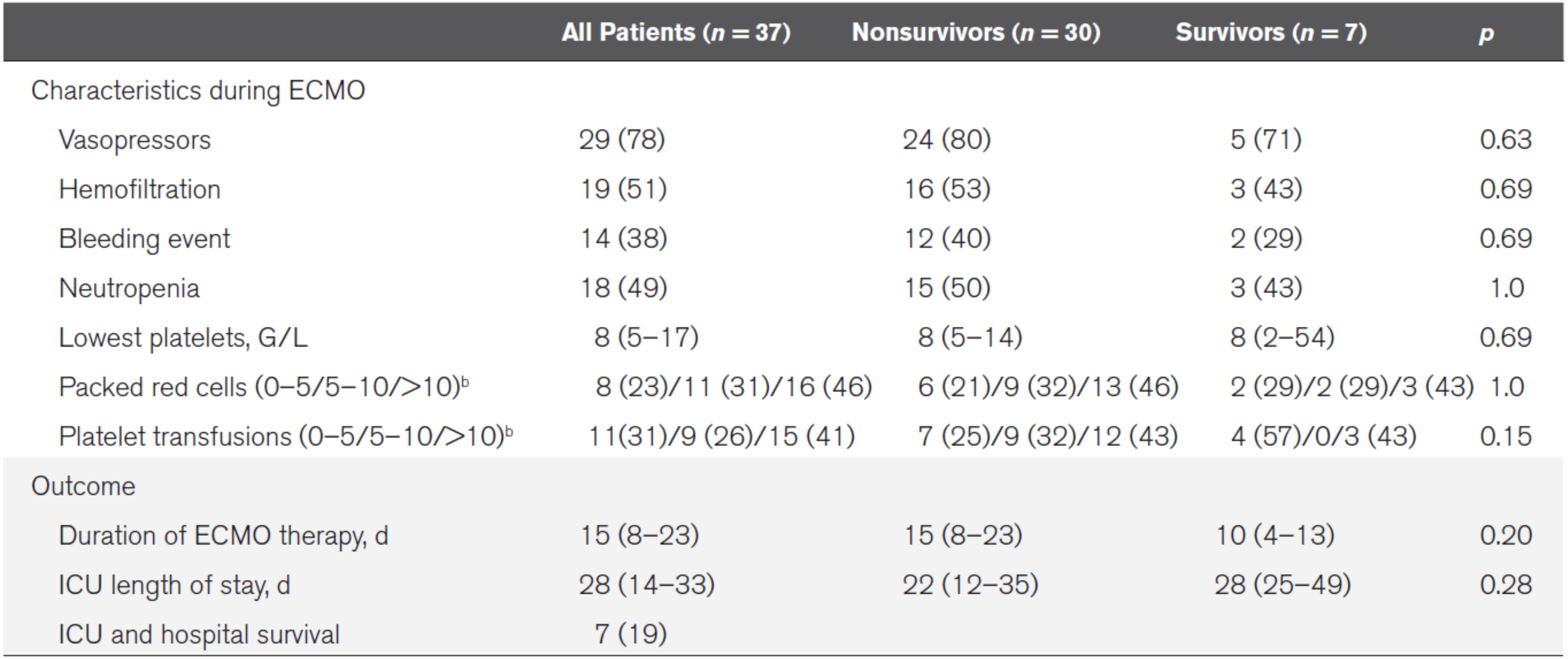
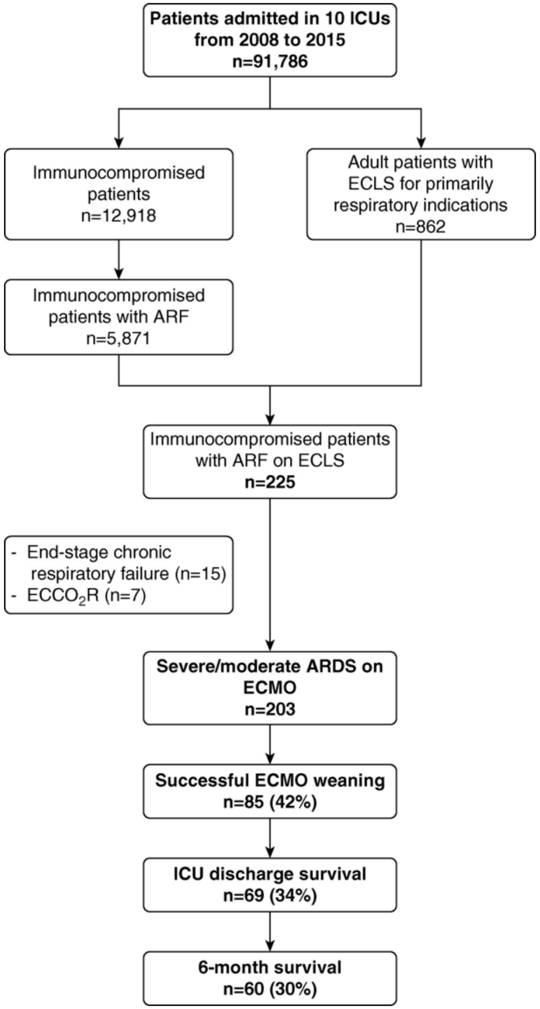


	All Patients ($n = 37$)	Nonsurvivors ($n = 30$)	Survivors ($n = 7$)	p
Characteristics during ECMO				
Vasopressors	29 (78)	24 (80)	5 (71)	0.63
Hemofiltration	19 (51)	16 (53)	3 (43)	0.69
Bleeding event	14 (38)	12 (40)	2 (29)	0.69
Neutropenia	18 (49)	15 (50)	3 (43)	1.0
Lowest platelets, G/L	8 (5–17)	8 (5–14)	8 (2–54)	0.69
Packed red cells (0–5/5–10/>10)[b]	8 (23)/11 (31)/16 (46)	6 (21)/9 (32)/13 (46)	2 (29)/2 (29)/3 (43)	1.0
Platelet transfusions (0–5/5–10/>10)[b]	11(31)/9 (26)/15 (41)	7 (25)/9 (32)/12 (43)	4 (57)/0/3 (43)	0.15
Outcome				
Duration of ECMO therapy, d	15 (8–23)	15 (8–23)	10 (4–13)	0.20
ICU length of stay, d	28 (14–33)	22 (12–35)	28 (25–49)	0.28
ICU and hospital survival	7 (19)			

Six-Month Outcome of Immunocompromised Patients with Severe Acute Respiratory Distress Syndrome Rescued by Extracorporeal Membrane Oxygenation

An International Multicenter Retrospective Study

Matthieu Schmidt[1,2], Peter Schellongowski[3], Nicolò Patroniti[4], Fabio Silvio Taccone[5], Dinis Reis Miranda[6], Jean Reuter[7], Helène Prodanovic[8], Marc Pierrot[9], Amandine Dorget[2], Sunghoon Park[10], Martin Balik[11], Alexandre Demoule[8], Ilaria Alice Crippa[5], Alain Mercat[9], Philipp Wohlfarth[3], Romain Sonneville[7], and Alain Combes[1,2]; for the International ECMO Network (ECMONet), the REVA Research Network, and the IDEA Study Group



Patients admitted in 10 ICUs from 2008 to 2015 n=91,786

Immunocompromised patients n=12,918

Adult patients with ECLS for primarily respiratory indications n=862

Immunocompromised patients with ARF n=5,871

Immunocompromised patients with ARF on ECLS **n=225**

- End-stage chronic respiratory failure (n=15)
- $ECCO_2R$ (n=7)

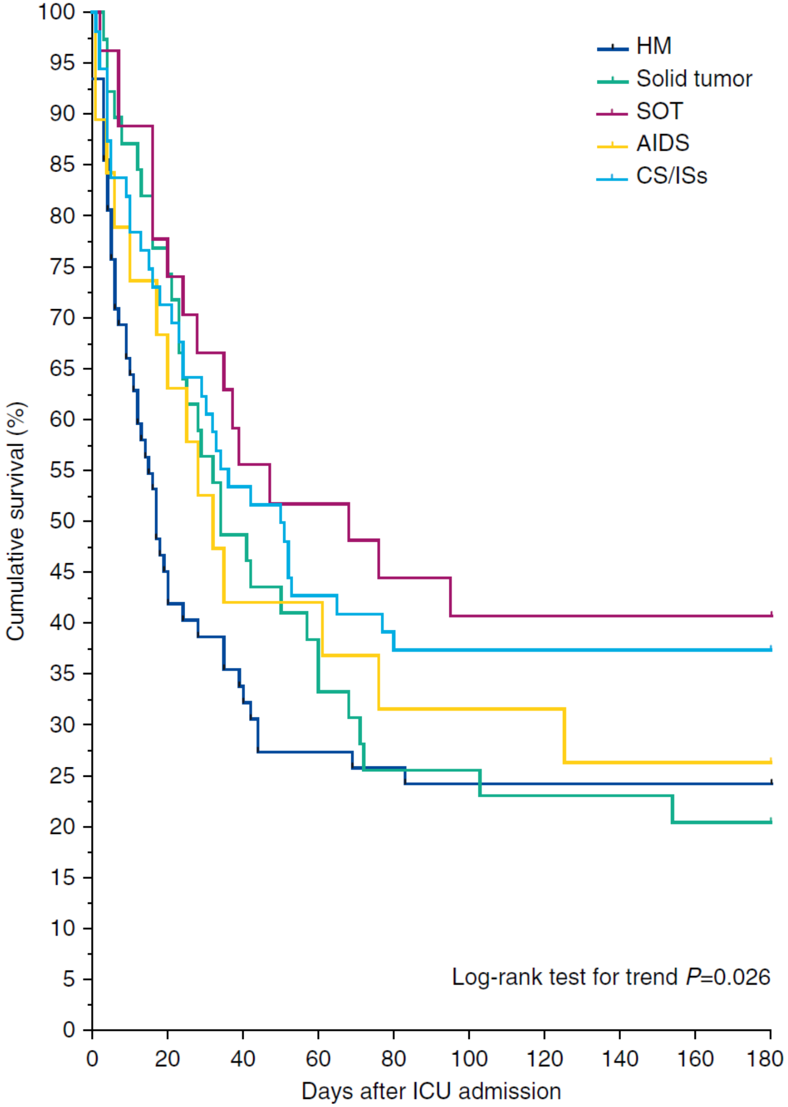
Severe/moderate ARDS on ECMO n=203

Successful ECMO weaning n=85 (42%)

ICU discharge survival n=69 (34%)

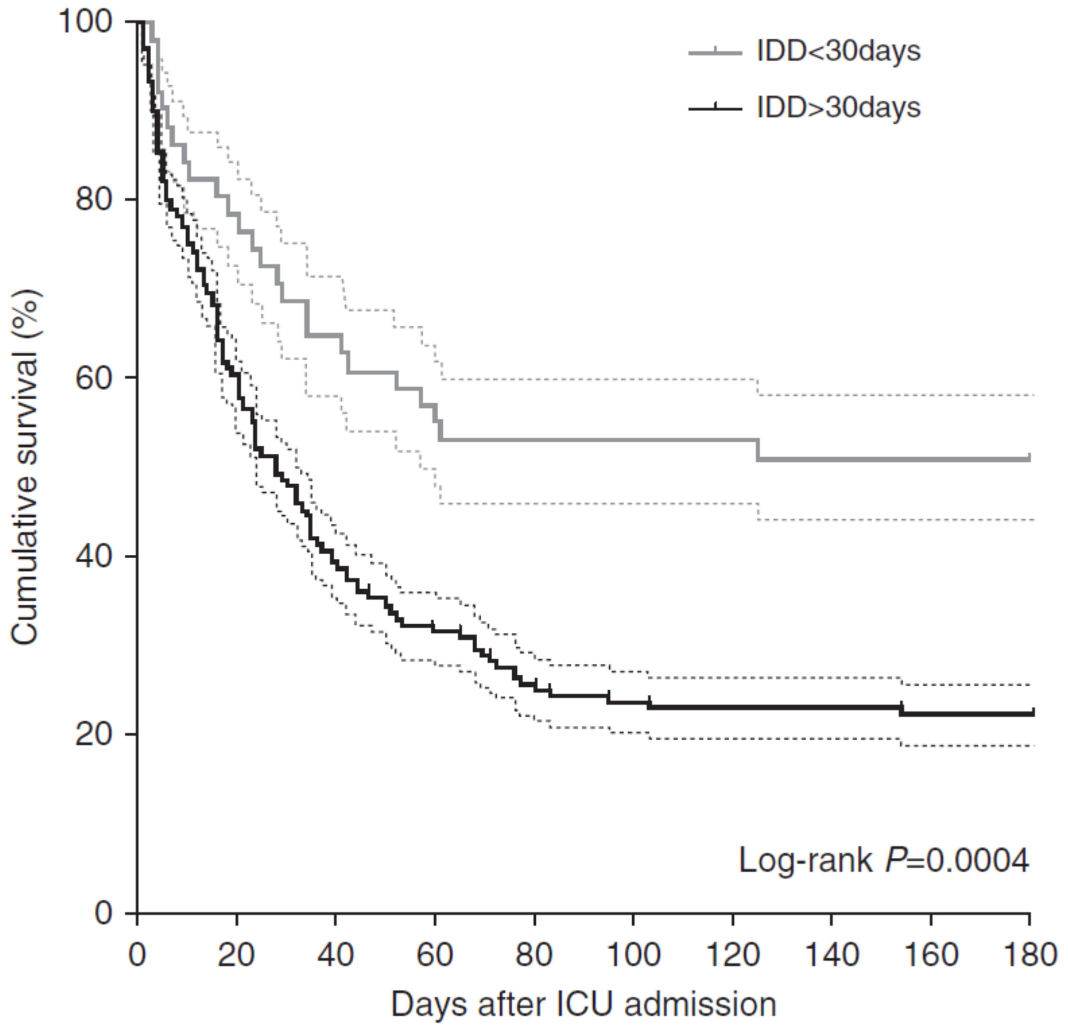
6-month survival n=60 (30%)

American Journal of Respiratory and Critical Care Medicine Volume 197 Number 10 | May 15 2018



HM	62	26	20	17	16	15	15	15	15	15
Solid tumor	39	29	19	13	10	10	09	09	08	08
SOT	27	20	15	14	12	11	11	11	11	11
AIDS	19	12	08	08	06	06	06	05	05	05
CS/ISs	56	40	30	24	21	21	21	21	21	21

Figure 2. Kaplan-Meier estimates during the 180 days after ICU admission, depending on patients' underlying immunodeficiency. CS = corticosteroids; HM = hematological malignancies; IS = immunosuppressant use; SOT = solid-organ transplant.



IDD<30d	51	39	33	28	27	27	27	26	26	26
IDD>30d	152	88	59	48	38	36	35	35	34	34

Figure 3. Kaplan-Meier survival estimates for immunocompromised patients with refractory acute respiratory distress syndrome on extracorporeal membrane oxygenation 180 days after ICU admission, according to the time of immunodeficiency diagnosis (IDD) (<30 or >30 d) (log-rank test; *P* = 0.0004). The dashed lines represent the 95% confidence interval.

Table 4. Pre-ECMO Predictors of 6-Month Mortality of Immunocompromised Patients with ARDS Rescued by ECMO

Variable*	**OR (95% CI)**	***P* Value**
Recently diagnosed immunodeficiency[†]	0.364 (0.148–0.899)	0.028
Platelet count	0.996 (0.992–0.999)	0.008
P_{CO_2}	1.031 (1.005–1.058)	0.019
Age	1.032 (1.002–1.062)	0.035
Driving pressure	1.079 (1.001–1.164)	0.047

Definition of abbreviations: ARDS = acute respiratory distress syndrome; CI = confidence interval; ECMO = extracorporeal membrane oxygenation; OR = odds ratio.

*Obtained for 134 patients with complete data.

[†] A recently diagnosed immunocompromised status was defined as confirmed fewer than 30 days before ICU admission.

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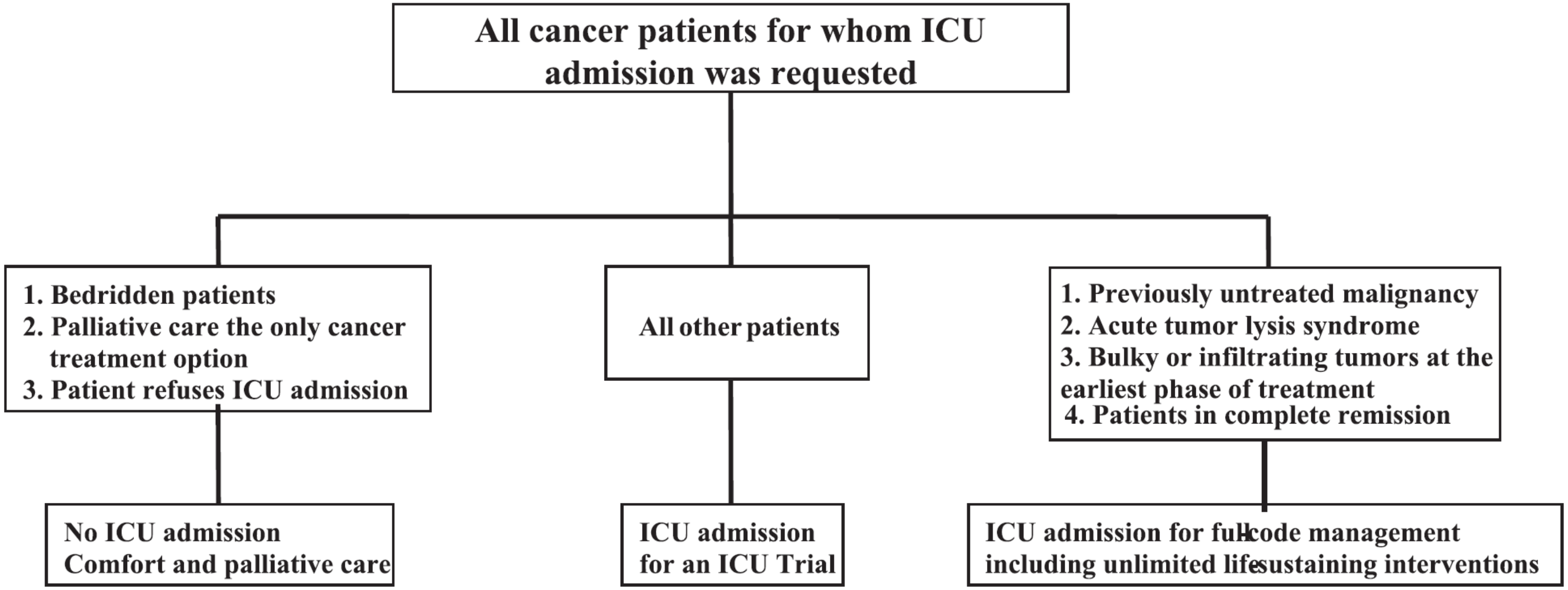
Qui admettre?

The ICU Trial: A new admission policy for cancer patients requiring mechanical ventilation*

Lucien Lecuyer, MD; Sylvie Chevret, MD, PhD; Guillaume Thiery, MD; Michael Darmon, MD;
Benoît Schlemmer, MD; Élie Azoulay, MD, PhD



All cancer patients for whom ICU admission was requested

1. **Bedridden patients**
2. **Palliative care the only cancer treatment option**
3. **Patient refuses ICU admission**

All other patients

1. **Previously untreated malignancy**
2. **Acute tumor lysis syndrome**
3. **Bulky or infiltrating tumors at the earliest phase of treatment**
4. **Patients in complete remission**

No ICU admission
Comfort and palliative care

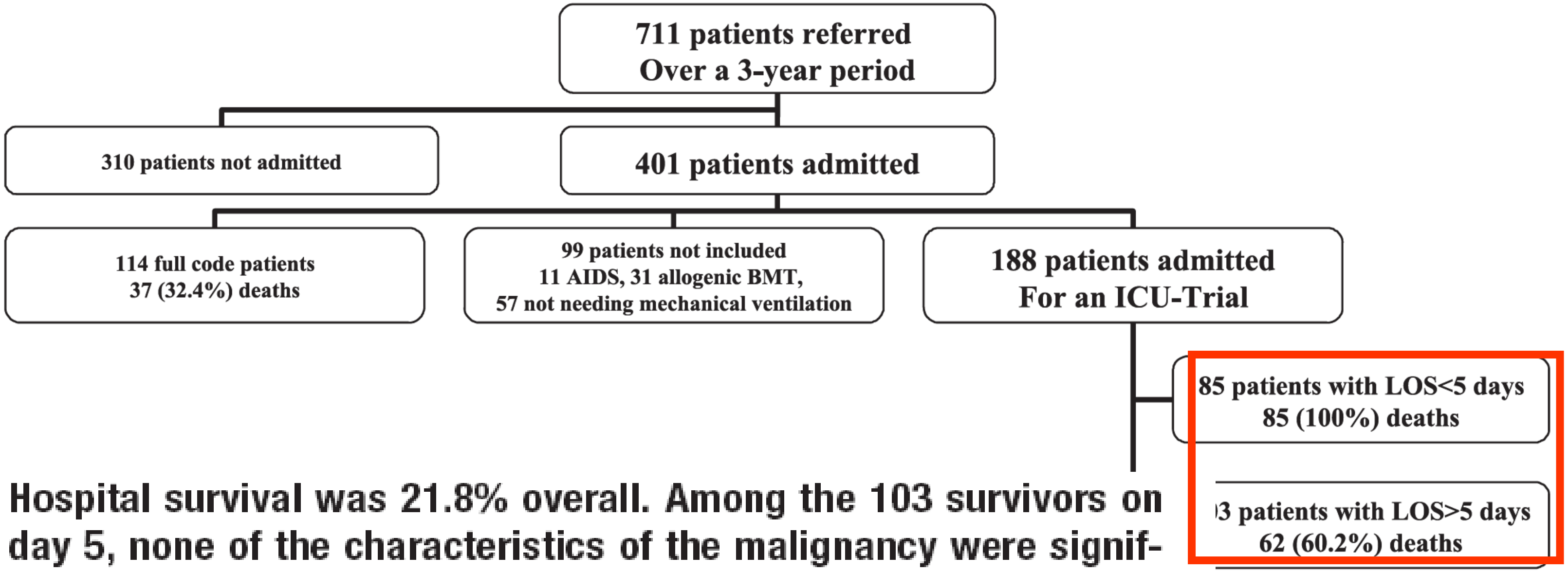
ICU admission
for an ICU Trial

ICU admission for full-code management
including unlimited life-sustaining interventions

ıre 1. Intensive care unit (*ICU*) admission policy initiated in 2001 at the Saint-Louis Hospital.

Crit Care Med 2007 Vol. 35, No. 3

Evolution/ré-évaluation



711 patients referred
Over a 3-year period

310 patients not admitted

401 patients admitted

114 full code patients
37 (32.4%) deaths

99 patients not included
11 AIDS, 31 allogenic BMT,
57 not needing mechanical ventilation

188 patients admitted
For an ICU-Trial

85 patients with LOS<5 days
85 (100%) deaths

3 patients with LOS>5 days
62 (60.2%) deaths

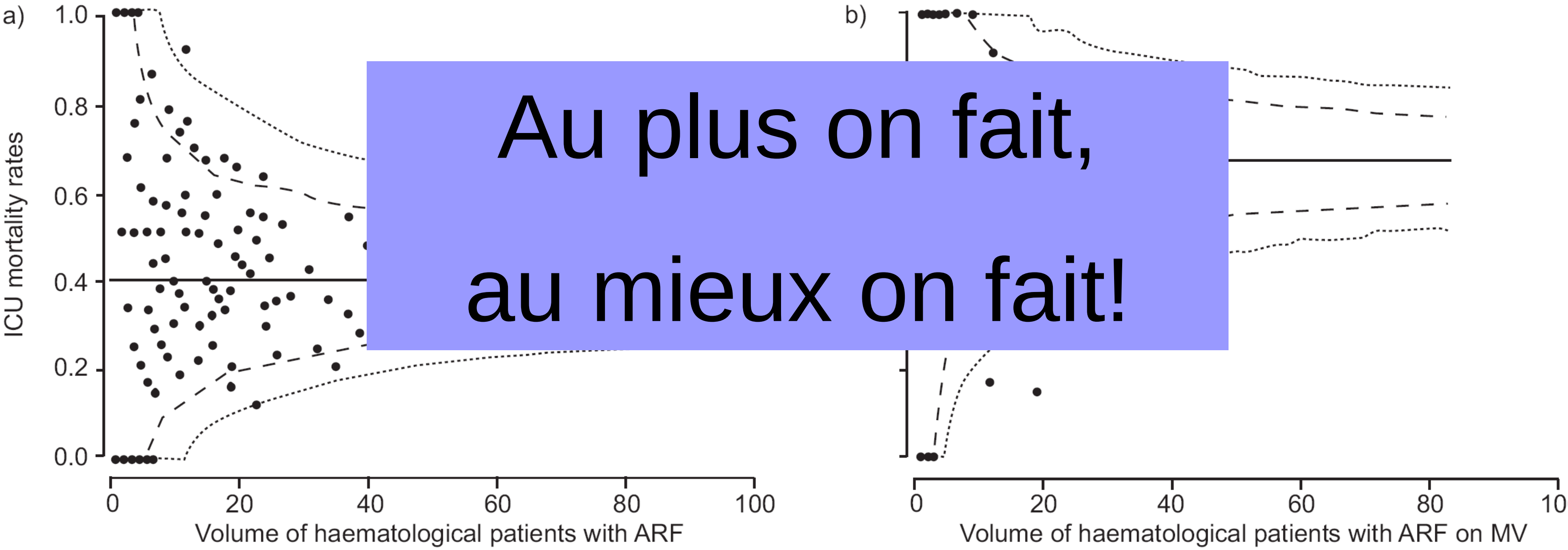
ure 2. P

Hospital survival was 21.8% overall. Among the 103 survivors on day 5, none of the characteristics of the malignancy were significantly different between the 62 patients who died and the 41 who survived. Time course of organ dysfunction over the first 6 ICU days differed significantly between survivors and nonsurvivors. Organ failure scores were more accurate on day 6 than at admission or on day 3 for predicting survival. All patients who required initiation of mechanical ventilation, vasopressors, or dialysis after 3 days in the ICU died.

Comment faire mieux?

Case volume and mortality in haematological patients with acute respiratory failure

154563 critically ill patients



Au plus on fait,

au mieux on fait!

521 patients did not require ventilatory support Mortality rate 6.90%	265 patients required noninvasive mechanical ventilation Mortality rate 11.69%	967 patients required invasive mechanical ventilation Mortality rate 66.7%

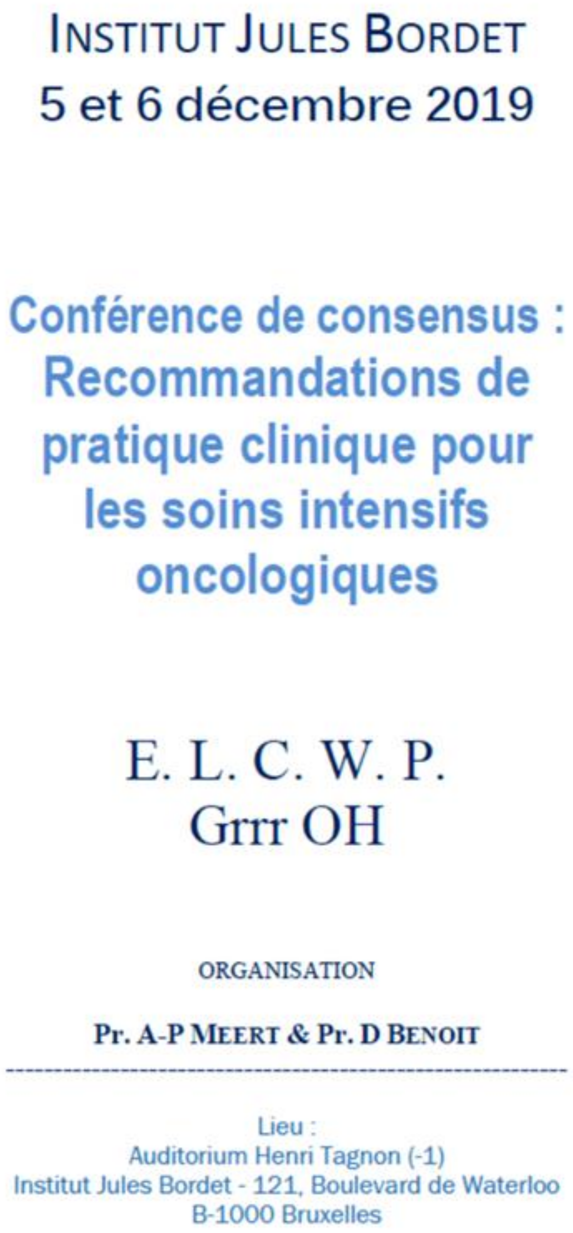
Eur Respir J 2008; 32: 748–754

Conclusions

- 50% patients onco-hémato
- Mortalité hospitalière diminue
  - meilleure technique de VMI
  - meilleure stratégie diagnostique
  - meilleure prise en charge de la complication
  - meilleur triage

Conclusions

- La VNI doit être utilisée avec précaution et évitée dans les hypoxémies sévères
- L’OHD ne diminue pas la mortalité en comparaison avec l’O2
- L’ECMO ne peut être envisagée que en cas de SDRA sévère et si le pronostic oncologique est acceptable



INSTITUT JULES BORDET

5 et 6 décembre 2019

Conférence de consensus : Recommandations de pratique clinique pour les soins intensifs oncologiques

E. L. C. W. P.

Grrr OH

ORGANISATION

Pr. A-P MEERT & Pr. D BENOIT

Lieu :
Auditorium Henri Tagnon (-1)
Institut Jules Bordet - 121, Boulevard de Waterloo
B-1000 Bruxelles

INSTITUT
JULES BORDET
INSTITUUT

ULB
iris

Jeudi 5 décembre 2019 de 14h à 18h

La prise en charge des patients d'onco-hématologie en réanimation est souvent basée sur des études de niveau de preuve faible sur base d'une littérature abondante mais parfois contradictoire, sur de petites études observationnelles relativement anciennes unicentriques avec une grande variabilité d'expérience selon les centres. Les spécificités de gestion de ces patients en réanimation nécessitent l'établissement de recommandations dédiées aux intensivistes. Le but de cette conférence de consensus est de fournir des recommandations de pratique clinique pour la prise en charge des patients atteints de cancer à l'USI sur la base d'une revue systématique de la littérature et d'avis d'experts.

Présidence :
Anne-Pascale Meert (Institut Jules Bordet, Bruxelles) &
Dominique Benoit (UZ, Gand)

- 14h-14h25 : *Introduction et méthodologie de la conférence de consensus* : Anne-Pascale Meert (Institut Jules Bordet, Bruxelles)
- 14h25-14h45 : *Méthodologie de la recherche de littérature.* Valérie Durieux (ULB, Bruxelles)
- 14h45-15h45 : **Sur base de quels critères, en terme de complications et tenant compte de l'affection néoplasiques et d'éventuelles limitations thérapeutiques, doit-on admettre un patient OH en réanimation?**
  Revue de la littérature : Thierry Berghmans (Institut Jules Bordet, Bruxelles)
  Avis d'expert : Emmanuel Canet (CHU Nantes)
  Discussion

15h45 : Pause-café

- 16h-17h : **Quel support ventilatoire, pour quelles complications et dans quel environnement (OHD, VNI, VMI, ECMO)?**
  Revue de la littérature : Bogdan Grigoriu (Institut Jules Bordet, Bruxelles)
  Avis d'expert : A Demoule (Hôpital Universitaire Pitié-Salpêtrière, Paris)
  Discussion
- 17h-18h : **Quelles considérations spécifiques à l'OH doit-on intégrer dans les SI (flux laminaire, isolement, DAVI, AB, soins palliatifs?...)?**
  Revue de la littérature : Bogdan Grigoriu (Institut Jules Bordet, Bruxelles)
  Avis d'expert : David Schnell (CH Angoulème)
  Discussion

Accréditation demandée en médecine interne

Vendredi 6 décembre 2019 de 9h à 18h

Présidence :
Anne-Pascale Meert (Institut Jules Bordet, Bruxelles) &
Dominique Benoit (UZ, Gand)

- 9h-10h : **Quel support hémodynamique, pour quelles complications, et dans quel environnement ?**
  Revue de la littérature : Thierry Berghmans (Institut Jules Bordet, Bruxelles)
  Avis d'expert: Achille Kouatchet (CHU d'Angers)
  Discussion
- 10h-11h : **Quel bénéfice dans l'ACR et pour quelles complications?**
  Revue de la littérature : Thierry Berghmans (Institut Jules Bordet, Bruxelles)
  Avis d'expert: Louis Voigt (MSK, New York, USA)
  Discussion

11h : pause- café

- 11h30-12h30 : **Quelle surveillance intensive dans un contexte de traitement carcinologique (chirurgie, chimio...)?**
  Revue de la littérature : Thierry Berghmans (Institut Jules Bordet, ULB)
  Avis d'expert: Virginie Lemiale (Hôpital St Louis, Paris)
  Discussion

12h30 : pause-déjeuner

- 13h30-14h30 : **Quel support d'épuration extra-rénale, pour quelles complications et dans quel environnement ?**
  Revue de la littérature : Thierry Berghmans (Institut Jules Bordet, Bruxelles)
  Avis d'expert : M Darmon (Hôpital St Louis, Paris)
  Discussion
- 14h30-15h30 : **Considérations spécifiques pour les transfusions (globules rouges, plaquettes, globules blancs).**
  Revue de la littérature : Bogdan Grigoriu (Institut Jules Bordet, Bruxelles)
  Avis d'expert : Frédéric Pene (Hôpital Cochin, Paris)
  Discussion
- 15h30-16h30: **Quelle formation aux différentes spécialités pour une interaction optimale du patient en SI oncologiques?**
  Revue de la littérature : Thierry Berghmans (Institut Jules Bordet, Bruxelles)
  Avis d'expert : Etienne Lengline (Hôpital Saint Louis, Paris)
  Discussion

Débat final et discussion avec le public

Samedi 7 décembre 2019 de 9h à 17h

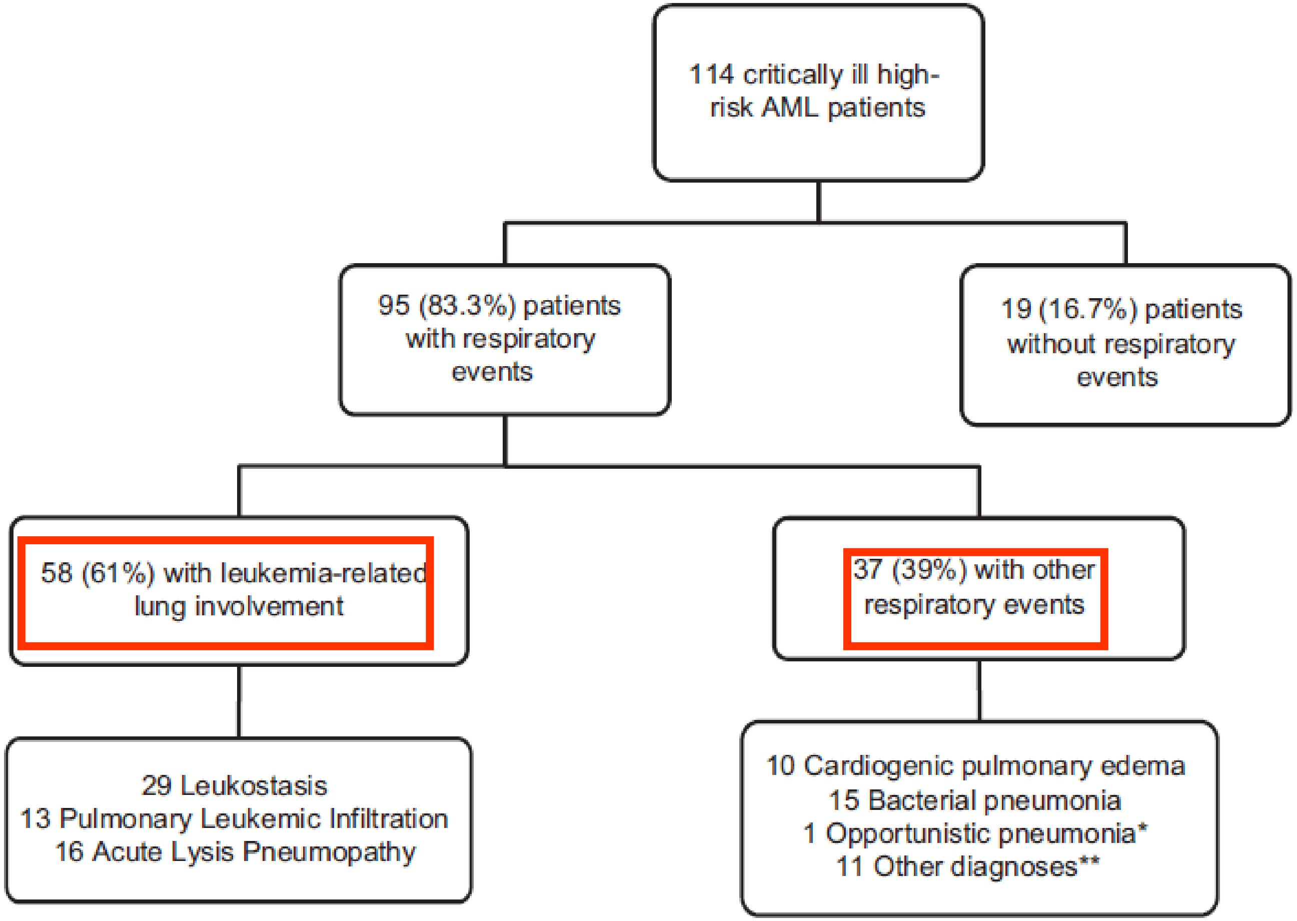
Réunion à huis clos du jury pour la rédaction des recommandations : Laurent Calvel, Stéphane Holbrechts, Jean-Jacques Lafitte, Nathalie Leclercq, France Lemaitre, Jean Lemaitre, Olivier Peyrony, Michaël Piagnerelli, Anne-Claire Toffart, Sebastian Wittnebel, Patient,

GRRROH (Groupe de Recherche en Réanimation Respiratoire en Onco-Hématologie)

www.grrroh.com

Respiratory events at the earliest phase of acute myeloid leukemia

Anne-Sophie Moreau[1], Etienne Lengline[2], Amélie Seguin[3], Virginie Lemiale[1], Emmanuel Canet[1],
Emmanuel Raffoux[2], Benoit Schlemmer[1] & Elie Azoulay[1]



114 critically ill high-risk AML patients

95 (83.3%) patients with respiratory events

19 (16.7%) patients without respiratory events

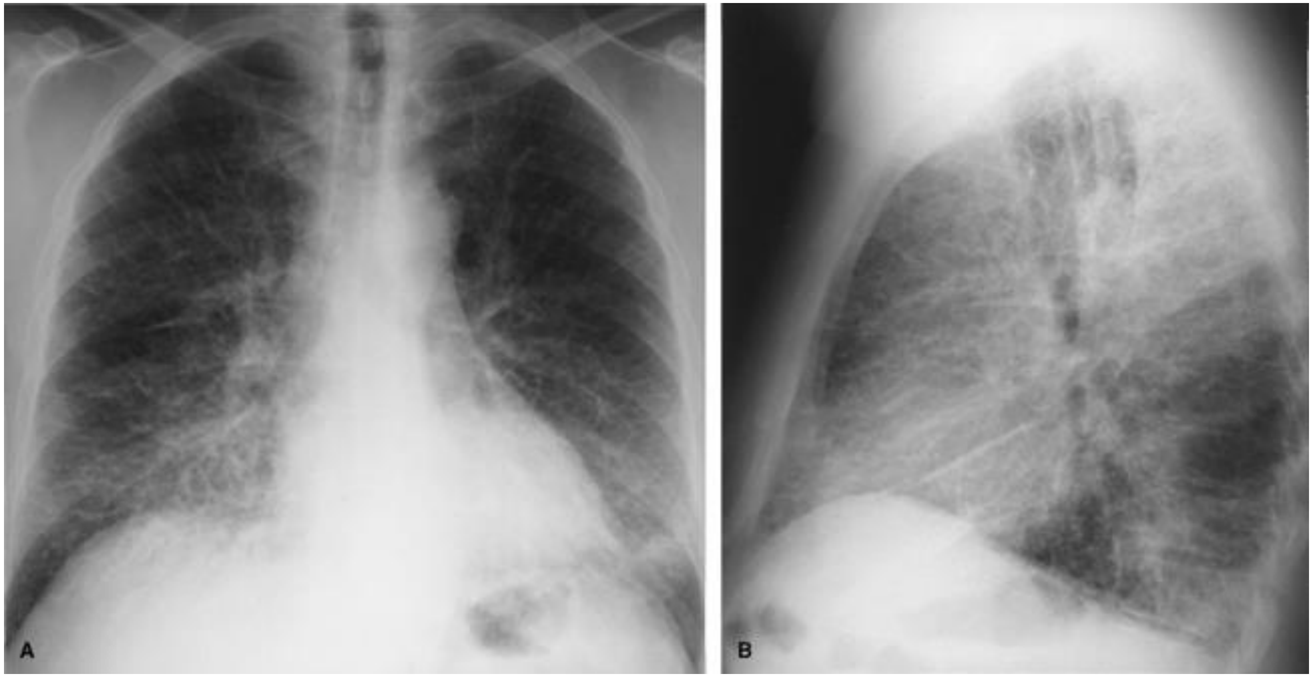
58 (61%) with leukemia-related lung involvement

37 (39%) with other respiratory events

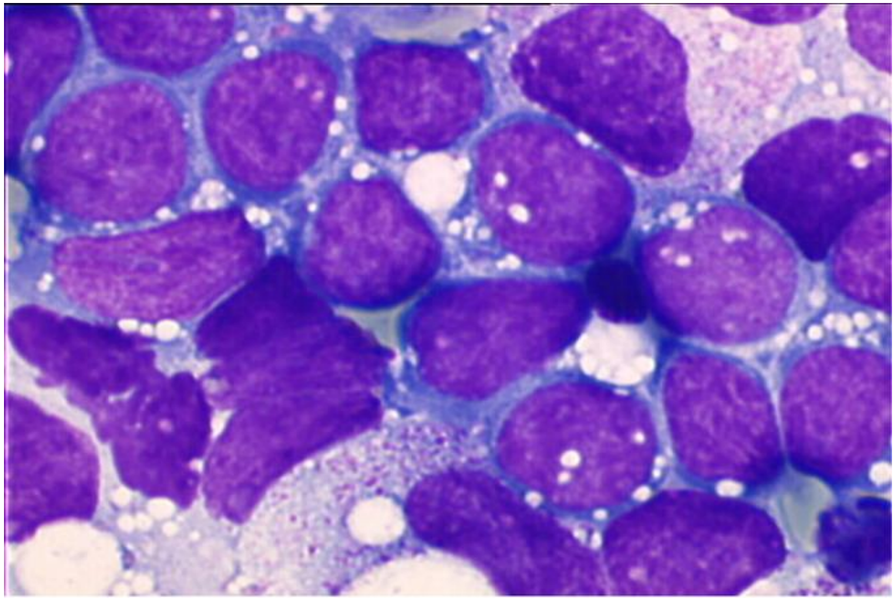
29 Leukostasis
13 Pulmonary Leukemic Infiltration
16 Acute Lysis Pneumopathy

10 Cardiogenic pulmonary edema
15 Bacterial pneumonia
1 Opportunistic pneumonia*
11 Other diagnoses**

Leukemia & Lymphoma, 2014; Early Online: 1–8

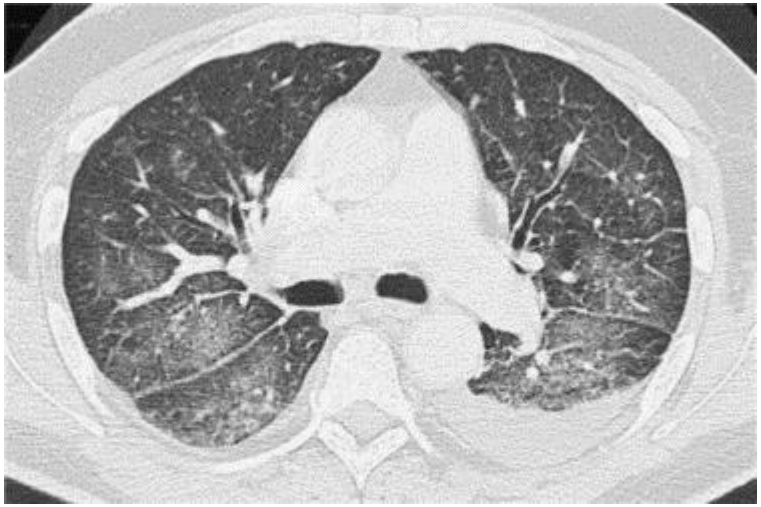


GB 130 000 GB



Infiltration pulmonaire leucémique

- LAM (4, 5) même si pas très hyperleucocytaire
- Localisation blastique extravasculaire tissulaire pulmonaire
- Syndrome interstitiel bilatéral à type d'opacités réticulaires de distribution lymphatique



Revue des Maladies Respiratoires, 589-598;2010,

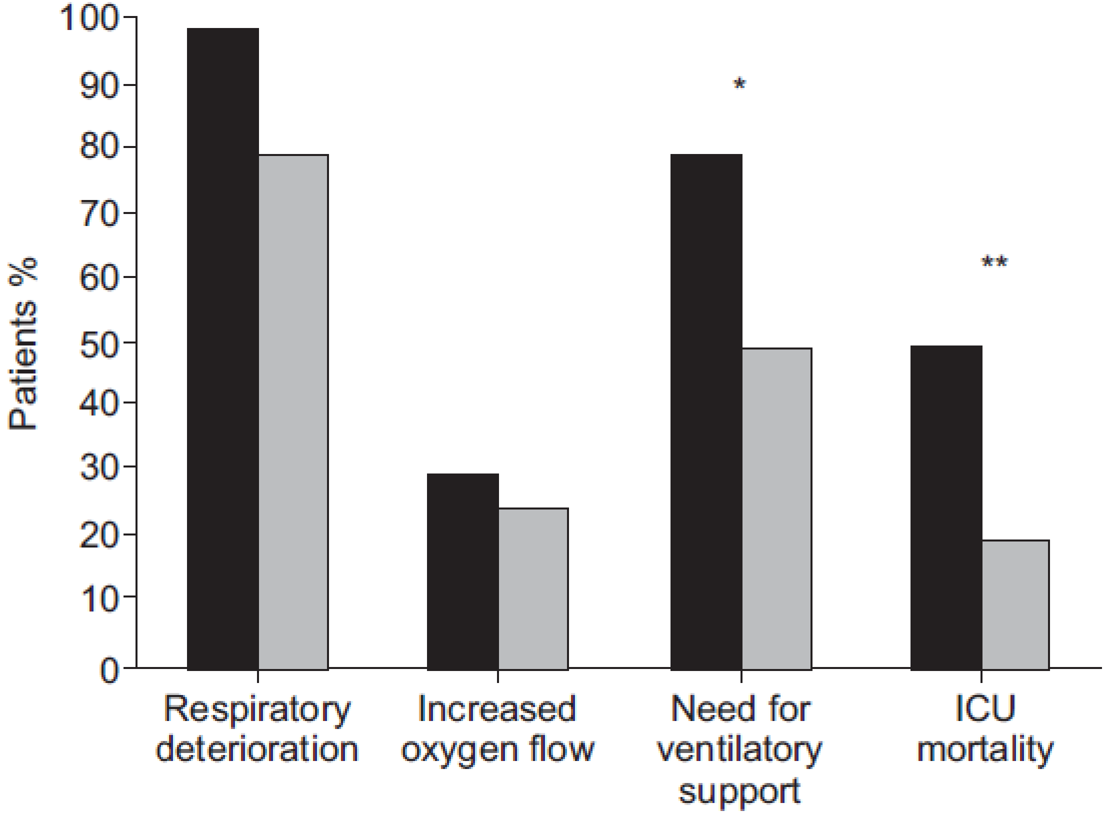
Pneumopathie de lyse tumorale

- complication rare
- atteinte alvéolaire diffuse
- Détresse respiratoire survenant avec l'initiation d'une chimiothérapie
- LAM (myélomonocytaire avec éosinophilie), LAL,
- 10 h à 20 jours après le début de la chimiothérapie
- SDRA , hémorragie alvéolaire.
- traitement supportif, avec recours éventuel à la ventilation

Eur Respir J 2012; 39: 648–653
DOI: 10.1183/09031936.00057711
Copyright©ERS 2012

Dexamethasone in patients with acute lung injury from acute monocytic leukaemia

**É. Azoulay*, E. Canet*, E. Raffoux#, E. Lengliné#, V. Lemiale*, F. Vincent*,
A. de Labarthe#, A. Seguin*, N. Boissel#, H. Dombret# and B. Schlemmer***



Causes d'IRA non infectieuses post allogreffe selon le Délai

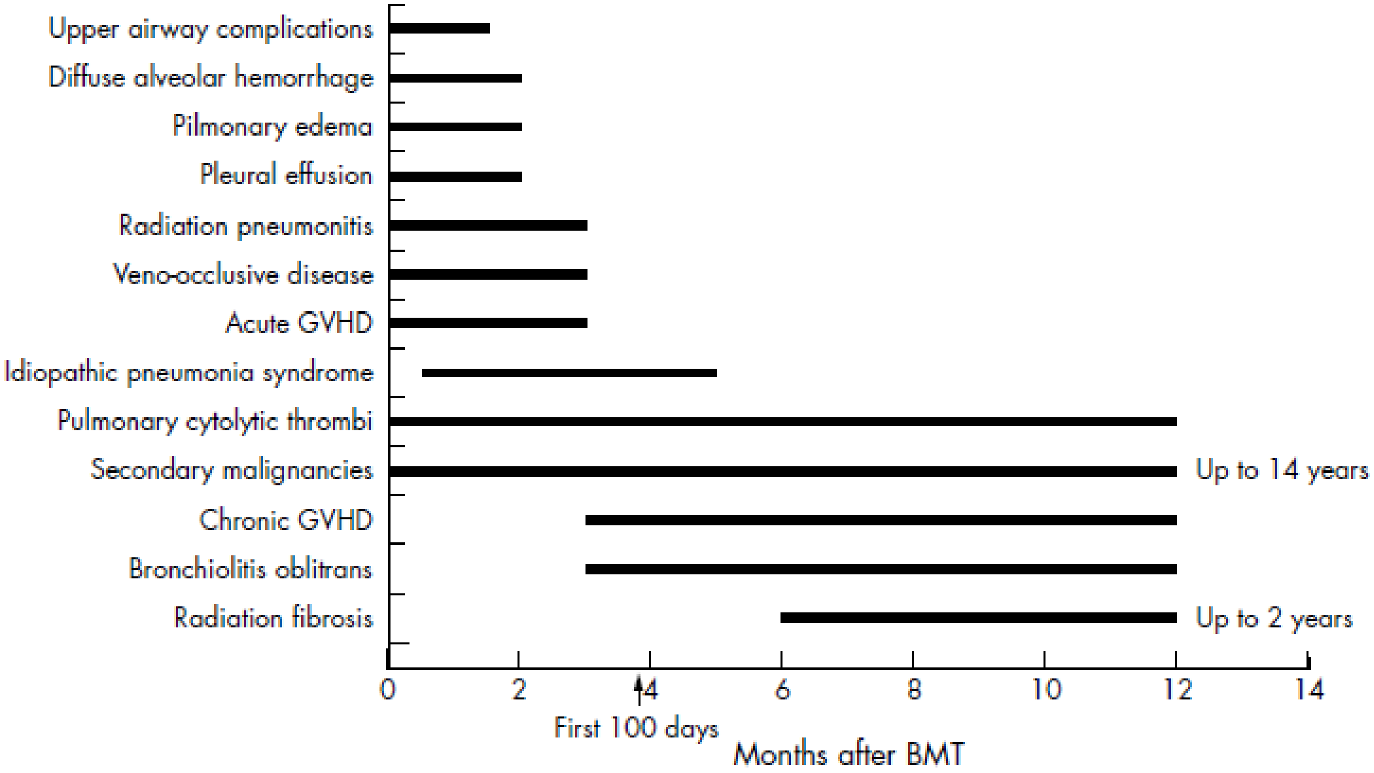
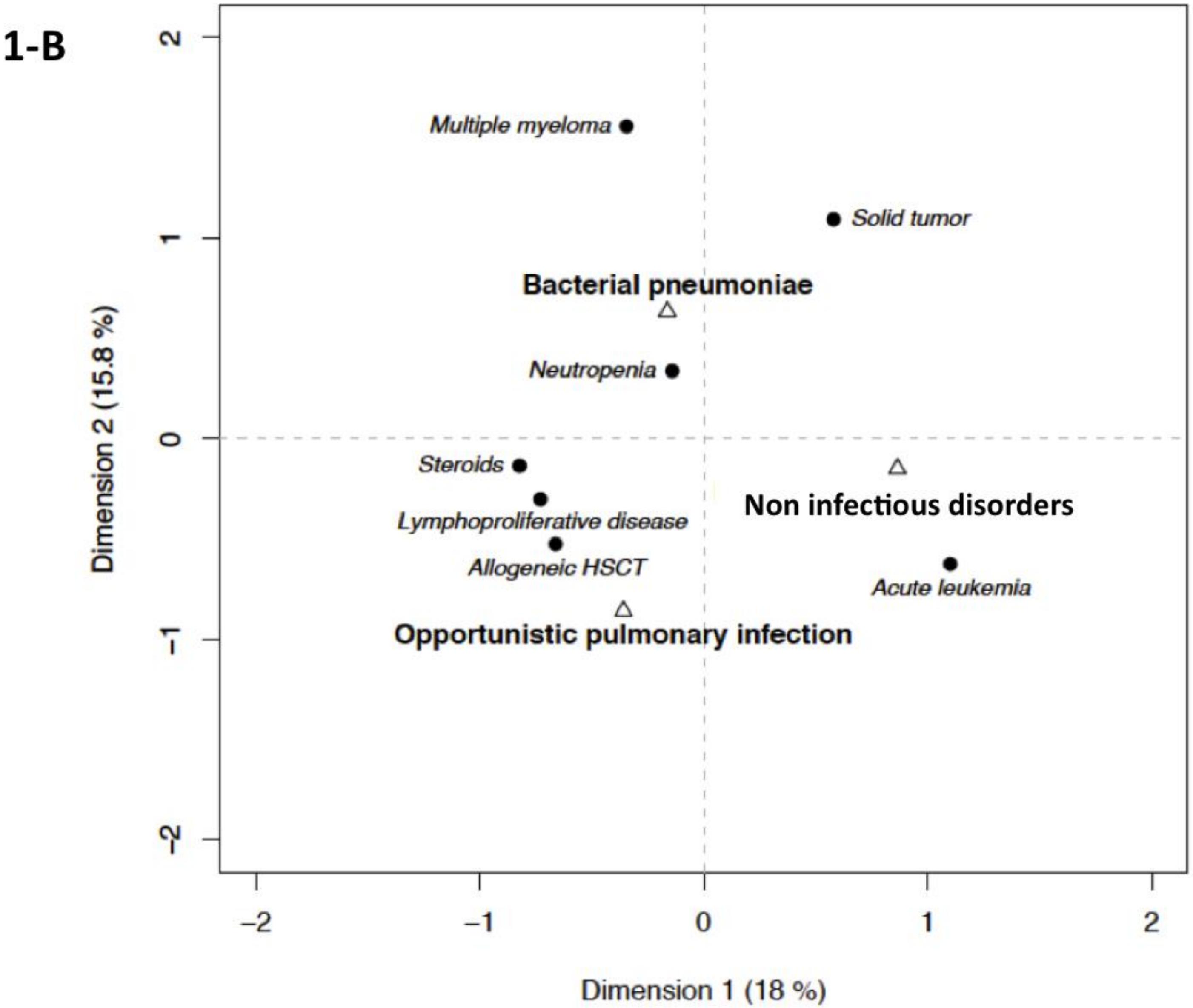


Figure 1 The chronology
non-infectious pulmonary complications after BMT.

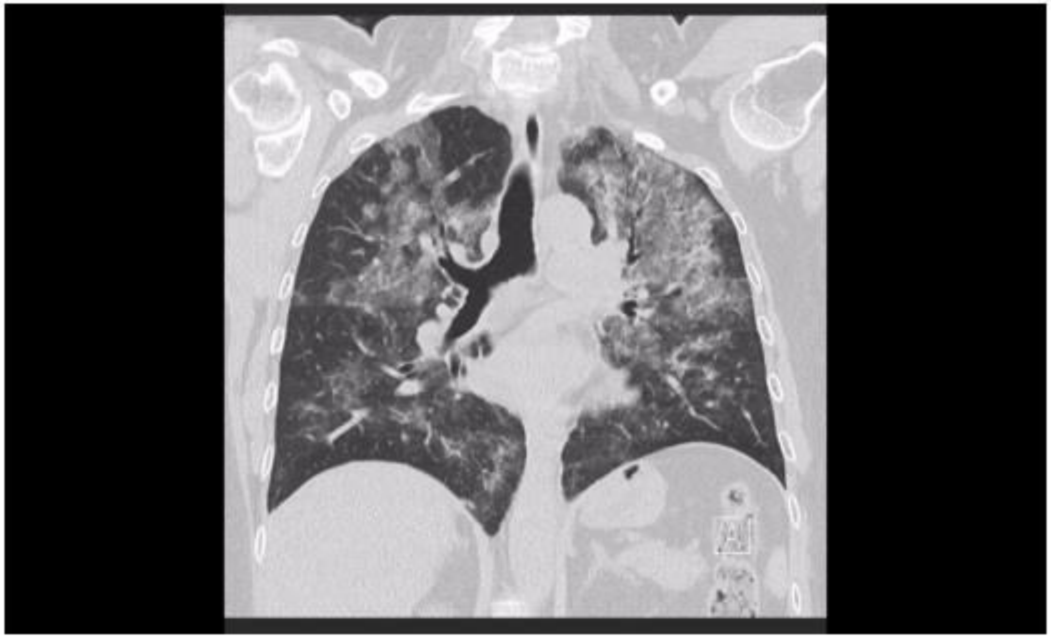
Causes d’IRA selon type d’Immunosuppression

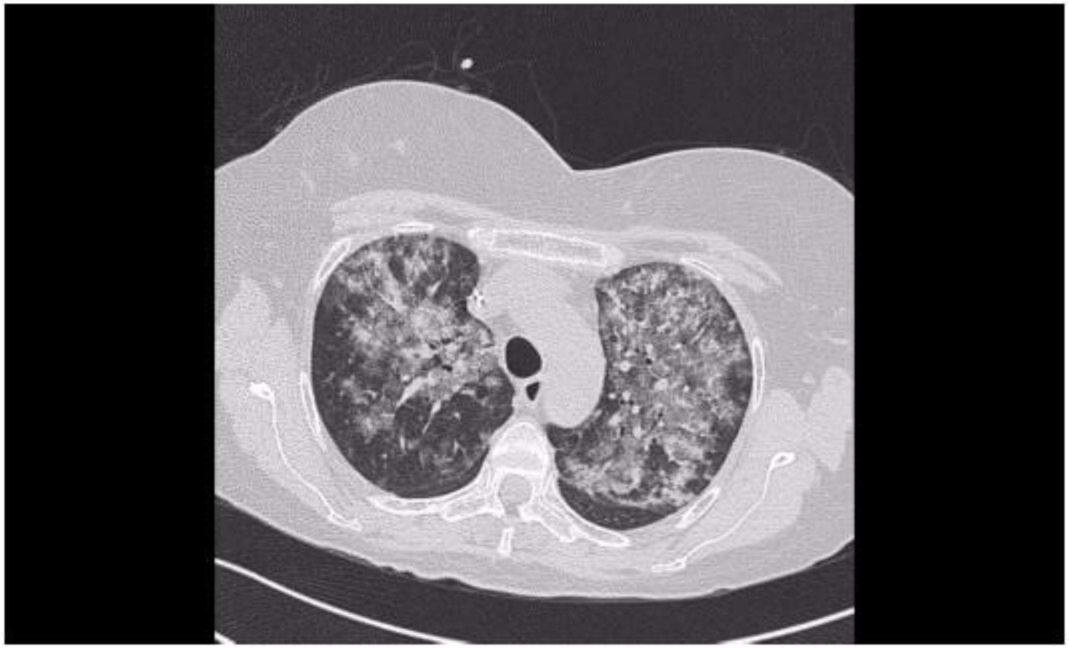


Causes d’IRA selon

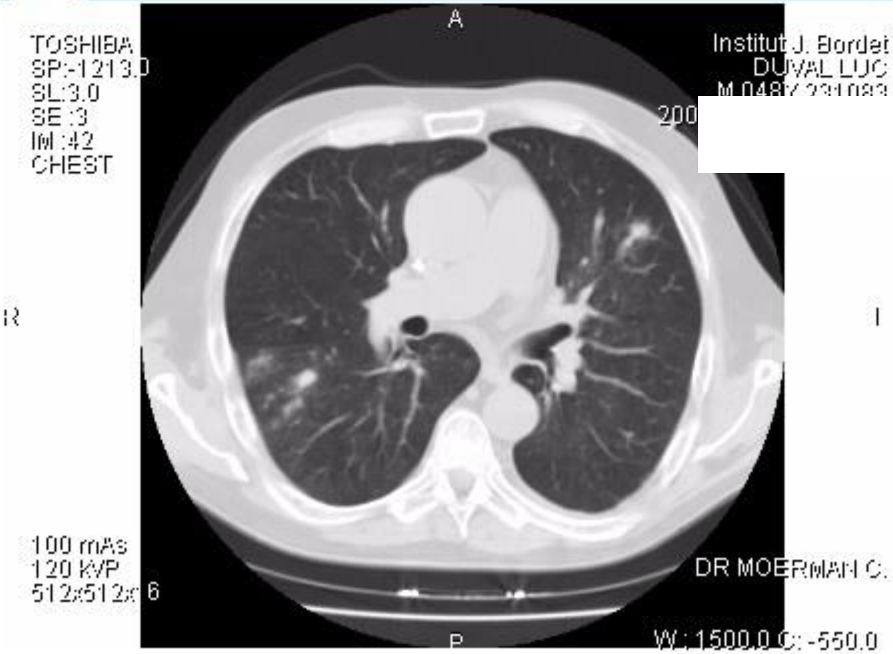
- Aspect Radiologique
- Expérience clinique
- Aspect CT

Femme de 53 ans
Néoplasie mammaire, avec des métastases hépatiques, osseuses et une métastase de la tige pituitaire; sous chimiothérapie par taxol+herceptine et corticoïdes ;
gazo(AA):7,52/32/50,
Lymphocytes=700/mm³





Homme 63 ans
LMC
Allogreffe haploidentique
GVH sous corticoïdes


A
TOSHIBA
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SL:3.0
SE:3
IM:42
CHEST
Institut J. Bordet
DUVAL LUC
M 048Y 231083
200 [redacted]
R
I
100 mAs
120 KVP
512x512x 6
DR MOERMAN C.
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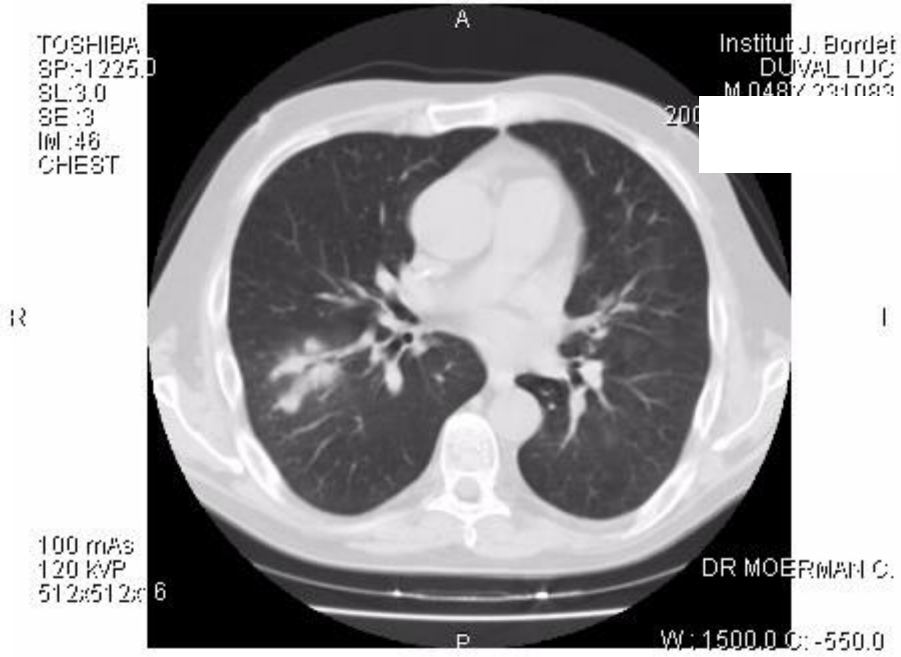
W: 1500.0 C: -550.0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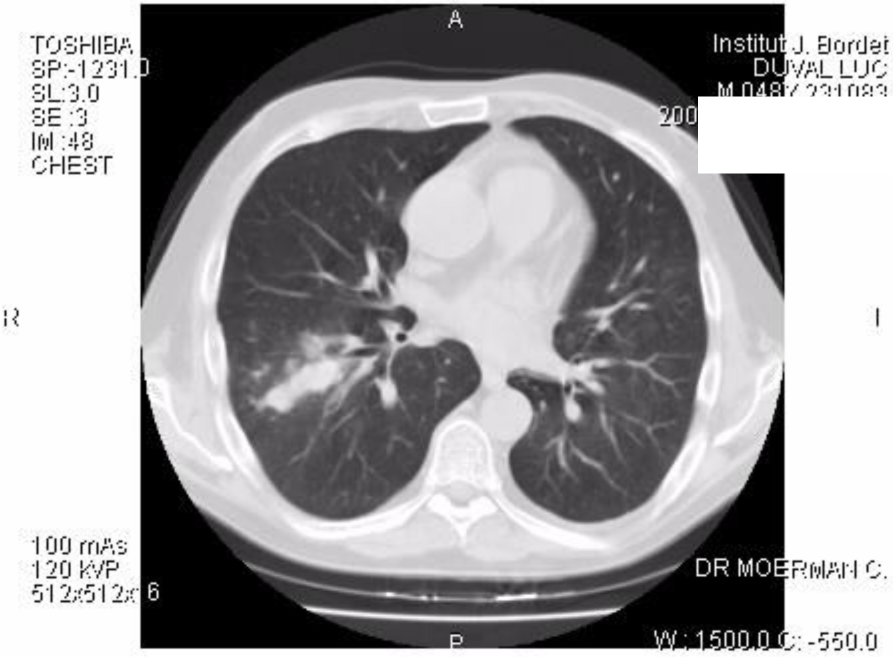
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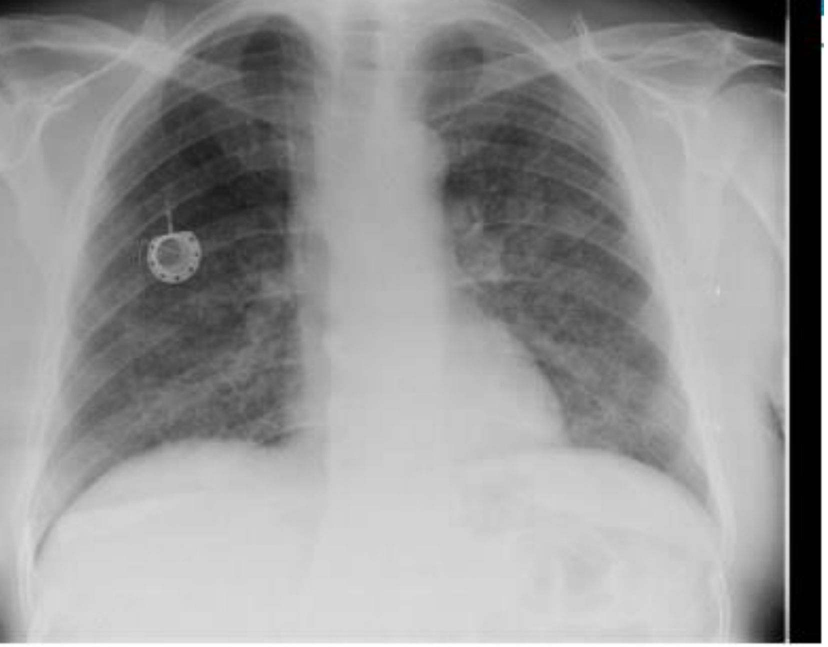
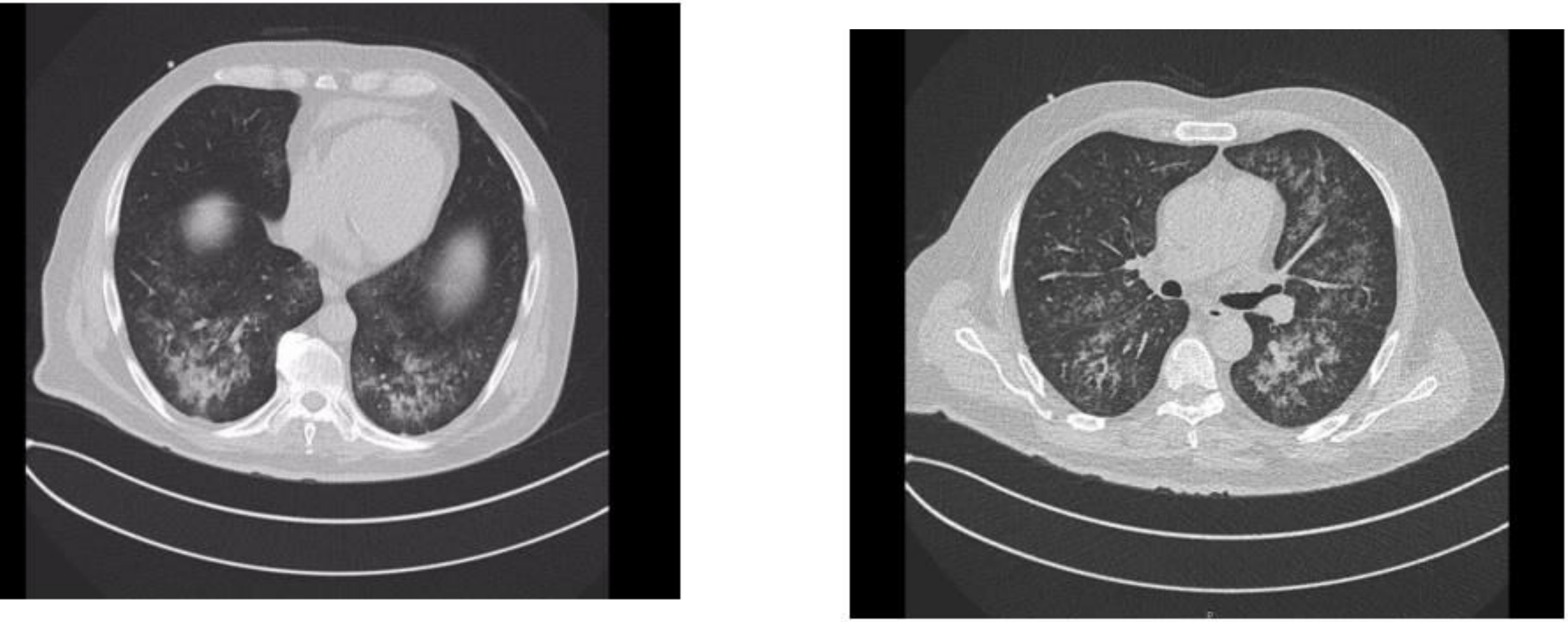
Institut J. Bordet
DUVAL LUC
M 048Y 231083
200 [redacted]
R
I
100 mAs
120 KVP
512x512x 6
DR MOERMAN C.
P
W: 1500.0 C: -550.0



Homme
59 ans allogreffe
LAL
sous Tacrolimus/
mycophenolate
Lymphopénie
Dyspnée

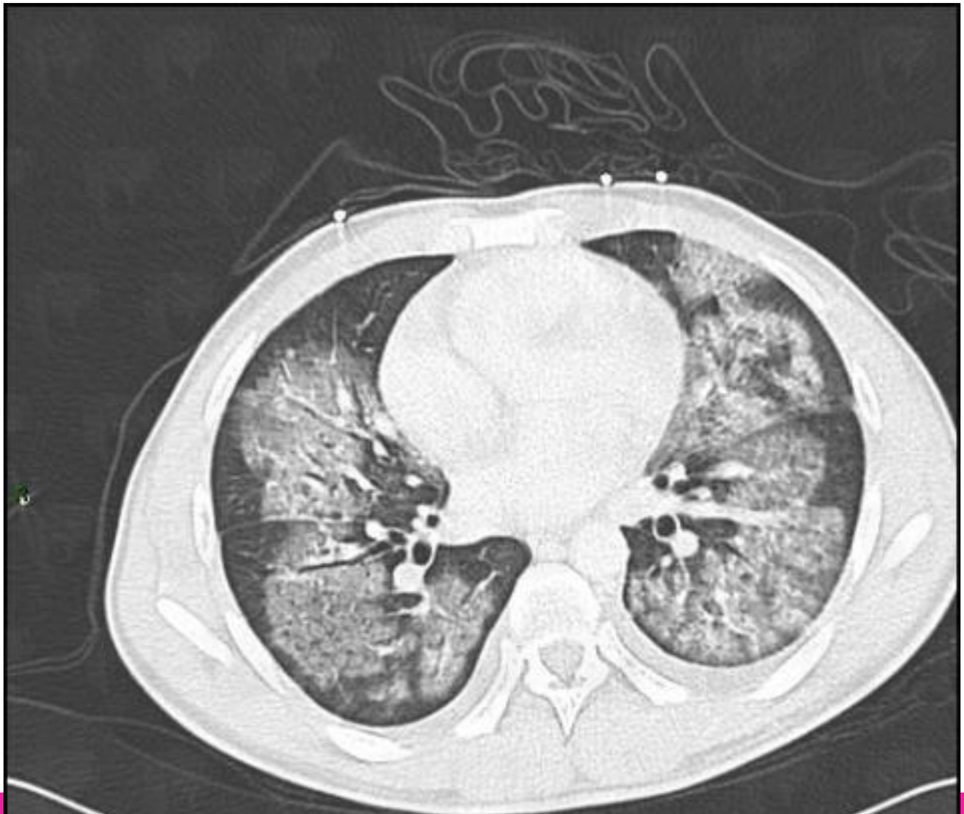


Homme 27 ans

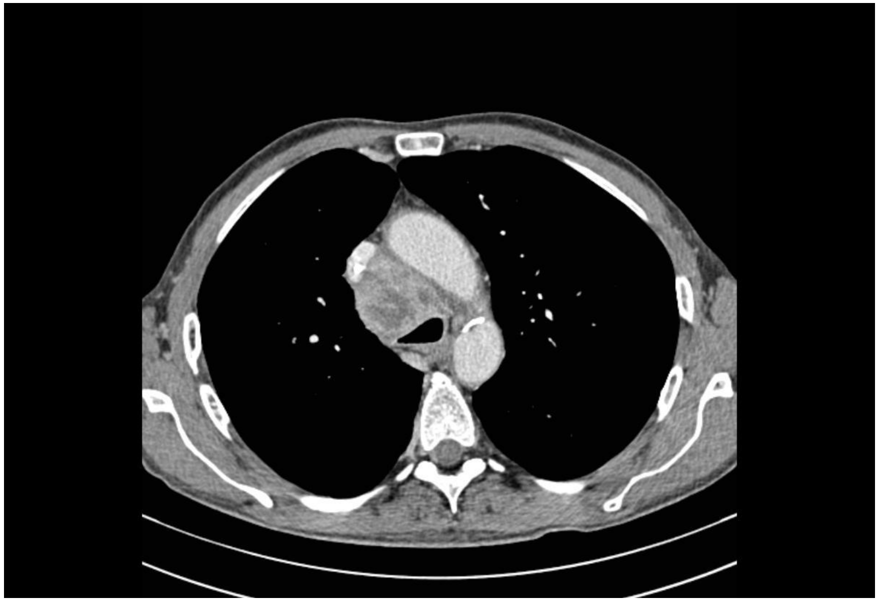
LAL allogreffe non familliale

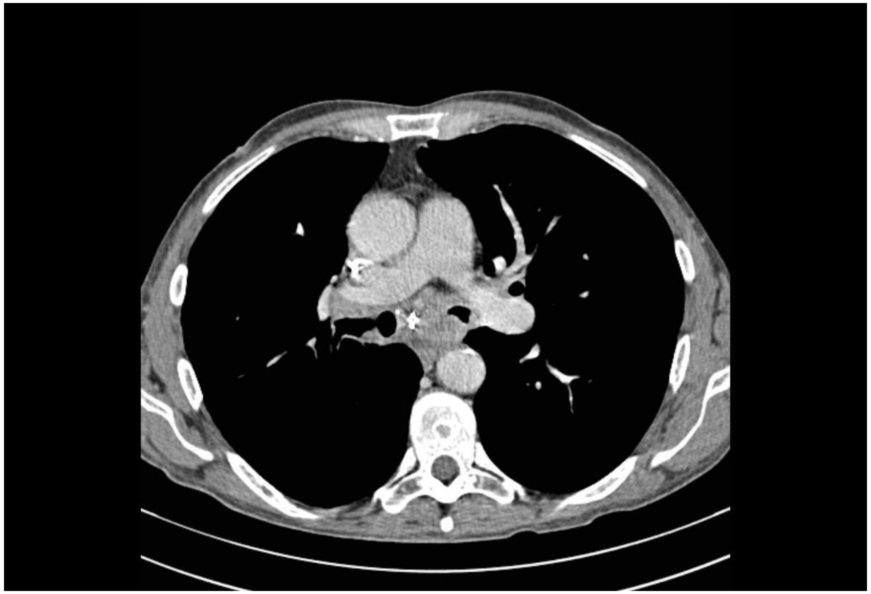
détresse respiratoire

contexte de pneumopathie, d'hypoplaquettose et de micro-angiopathie sur cysclosporine



Homme 47 ans.
Cancer bronchique.
Dyspnée inspiratoire.

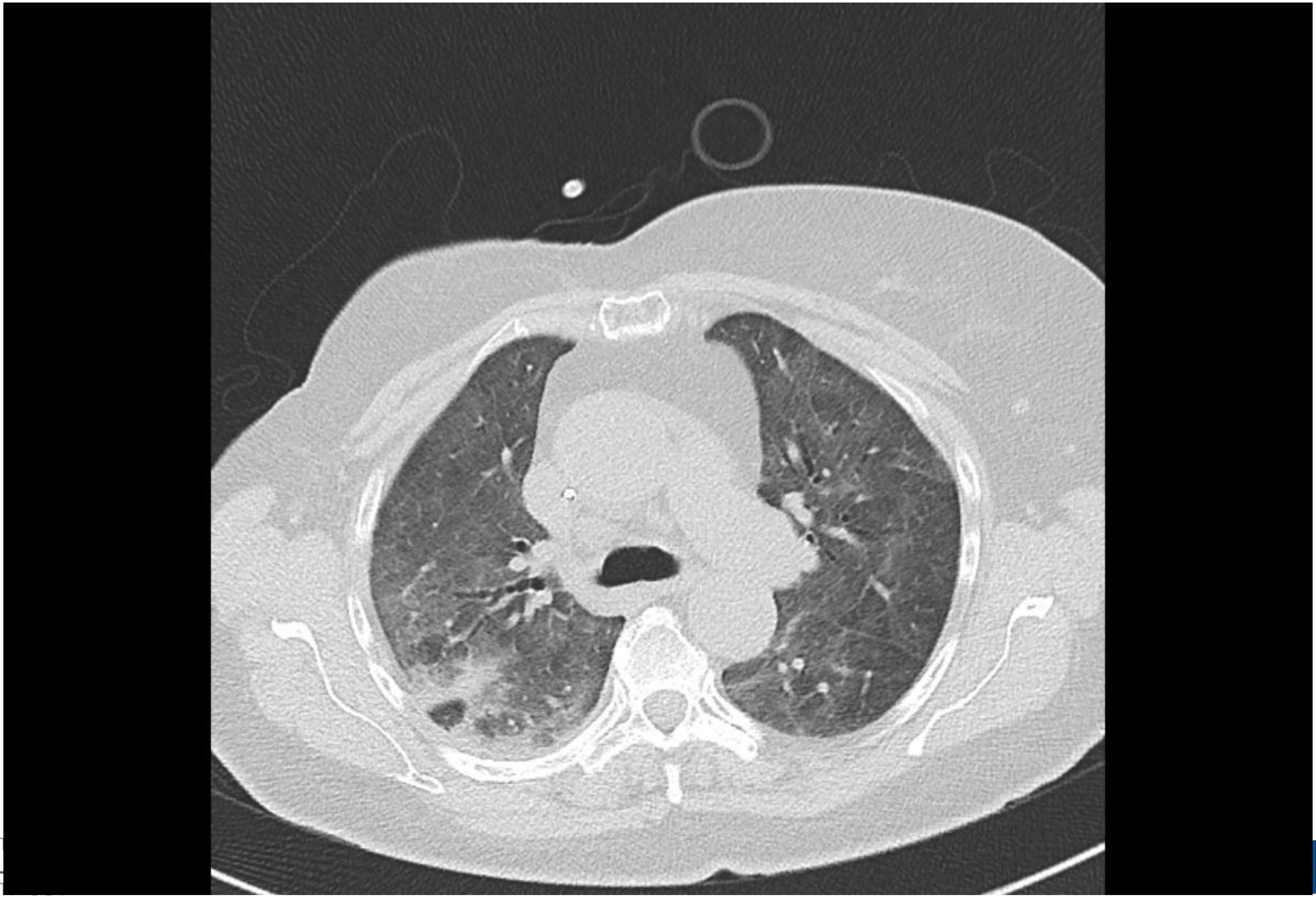




Embolie pulmonaire néoplasique/ lymphangite carcinomateuse

- embolisation de cellules néoplasiques dans les artères pulmonaires distales où elles sont résorbées pour infiltrer la vascularisation lymphatique, donnant le tableau de lymphangite carcinomateuse
- Dyspnée, douleurs thoraciques, toux et hémoptysies, SDRA, décompensation cardiaque droite
- CT thorax: signes de lymphangite, avec épaississement de l'interstice péribronchovasculaire et des septa.
- Chimiothérapie, corticoïdes?

Femme 68 ans.
Néoplasie mammaire M+ au niveau osseux traitée par Afinitor



Pneumonie interstitielle non spécifique	Gemcitabine, Fludarabine, Paclitaxel, Docetaxel, Irinotecan, Gefitinib, Erlotinib, Imatinib, Rituximab, Thalidomide, Bortezomib, Temsirolimus, Trastuzumab, Oxaliplatine, Temozolomide
Pneumonie d'hypersensibilité	Paclitaxel, Docetaxel, imatinib, méthotrexate
Pneumonie à éosinophiles	Fludarabine, Oxaliplatine
Fibrose interstitielle	Gemcitabine, Fludarabine, Paclitaxel, Gefitinib, oxaliplatine, bléomycine, mitomycine
Hémorragie alvéolaire	Gemcitabine, Gefitinib, Rituximab
Maladie veno-occlusive	Gemcitabine
Bronchiolite oblitérante	Topotecan, trastuzumab, thalidomide
DAD/SDRA	Fludarabine, docetaxel, oxaliplatine, gefitinib, erlotinib, gemcitabine, trastuzumab, Ara C
Epanchements pleuraux	Gemcitabine, fludarabine, docetaxel, imatinib, thalidomide
Bronchospasme	Gemcitabine, paclitaxel, anticorps monoclonaux
Hémoptysies	Bevacizumab

Management of Acute Complications of Targeted Therapy in Patients With Cancer: A Review of Cases Managed in ICU

Table 4. Case Reports of Life-Threatening Pulmonary Complications Leading Patient to the ICU.

Authors	Demographics, Treatment, and Indication	Life Threatening Complications	Management	Outcome
Créquit et al[33]	35-year-old man; crizotinib; NSCLC	ILD	Crizotinib stopped 3 weeks and reintroduction	Complete resolution; recurrence 11 months later
	48-year-old woman; crizotinib; NSCLC	ILD	Crizotinib stopped 4 weeks and reintroduction; corticosteroids 40 mg, progressively decreased to 5 mg	Regression of ILD
	51-year-old woman; crizotinib; NSCLC	ILD	Crizotinib stopped 3 weeks, reintroduced at 200 mg twice a day and antibiotics	Regression of ILD
	65-year-old man;Ccrizotinib; NSCLC	ILD	Crizotinib continued; antibiotics	Regression and recurrence 7 months later
	33-year-old man; crizotinib; NSCLC	ILD	Crizotinib continued; antibiotics, corticosteroids 40 mg progressively decreased to 5 mg	Regression and relapse of ILD 1 year later leading to increased corticosteroid posology
Ono et al[51]	63-year-old man; crizotinib; NSCLC	ILD	Crizotinib discontinuation; intubation and ventilation; Methylprednisolone 1 g/d; antibiotics	Death at day 89; autopsy: diffuse fibroproliferative phase alveolar damage
Tamiya et al[2]	39-year-old man; crizotinib; NSCLC	ILD	Crizotinib discontinuation; breathing oxygen mask; methylprednisolone 1 g/d during 3 days; antibiotics, *Pneumocystis jirovecii* treatment	Death at day 21; autopsy: diffuse alveolar damage
Yanagisawa et al[52]	53-year-old woman; crizotinib; NSCLC	ILD	Crizotinib discontinuation; methylprednisolone 1 g/d during 3 days	Regression of ILD; reintroduction of crizotinib 7 months later with intravenous dexamethasone 6.6 mg/d progressively decreased to 2 mg/d
Asai et al[53]	70-year-old woman; crizotinib; NSCLC	ILD	Crizotinib discontinuation for 2 weeks	Regression of ILD; reintroduction of crizotinib at 250 mg twice a day then increased at 400 mg twice a day, relapse of ILD and temporary stop of crizotinib
Ji et al[54]	53-year-old man; crizotinib; NSCLC	ILD	Crizotinib discontinuation; aggressive treatment (details not mentioned)	Death in 2 months; biopsy: acute interstitial lung disease
Tachihara et al[55]	70-year-old man; crizotinib; NSCLC	ILD	Crizotinib discontinuation for 1 week; careful observation	Flare of tumor growth conducting to restart crizotinib with prednisolone 20 mg/d; no ILD exacerbation, nor recurrence at 6 months of follow-up
Watanabe et al[3]	77-year-old man; crizotinib; NSCLC	ILD	Crizotinib discontinuation; methylprednisolone pulse; noninvasive positive pressure ventilation support	Death at day 16
van Geffen et al[35]	26-year-old woman; crizotinib; NSCLC	Respiratory failure because of a right-sided pneumonia and pulmonary embolism	ICU for noninvasive ventilation, antibiotics, and low-molecular-weight heparin in addition to crizotinib	Discharge after a week; good partial response with crizotinib
Sakhri et al[36]	35-year-old woman; erlotinib; NSCLC	Acute respiratory distress syndrome, secondary to a bilateral and spontaneous pneumothorax	Erlotinib stopped; intubation; thoracoscopic bilateral talc poudrage	Death by cancer progression

Journal of Intensive Care Medicine
1-14
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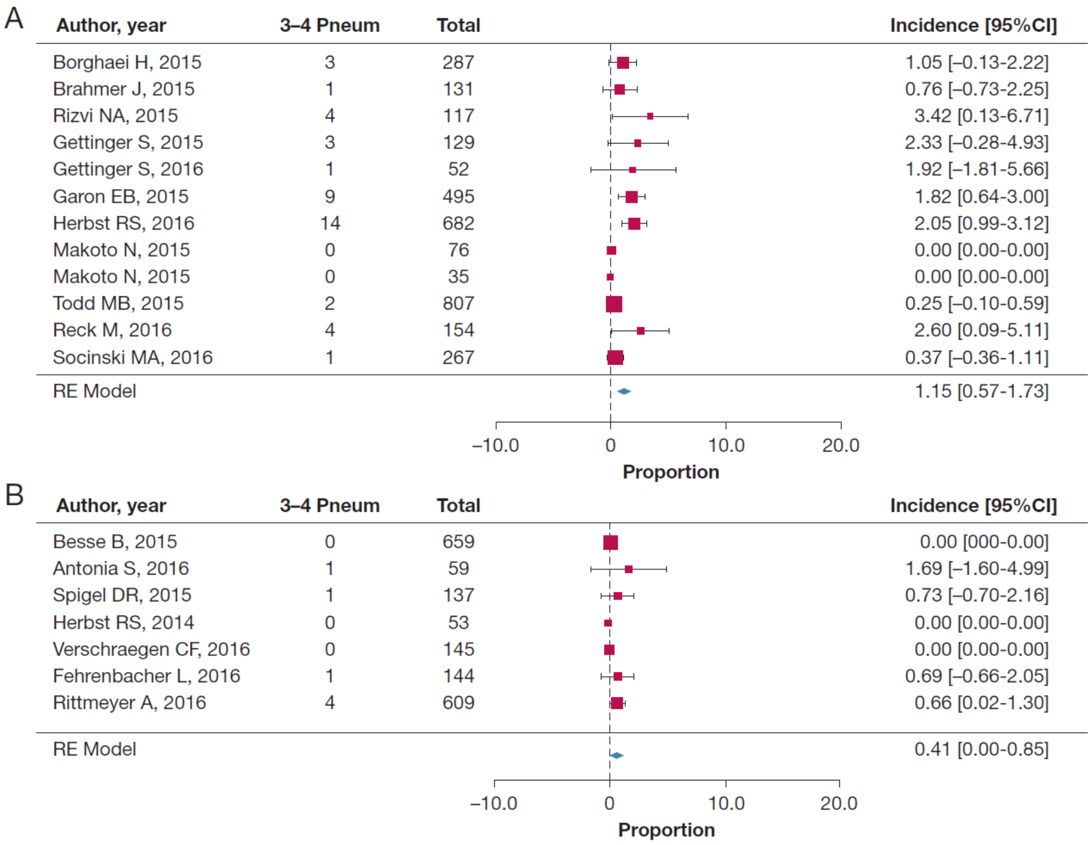
Incidence of Pneumonitis With Use of Programmed Death 1 and Programmed Death-Ligand 1 Inhibitors in Non-Small Cell Lung Cancer

A Systematic Review and Meta-Analysis of Trials

Monica Khunger, MD; Sagar Rakshit, MD; Vinay Pasupuleti, MD, PhD; Adrian V. Hernandez, MD, PhD;



A

Author, year	3–4 Pneum	Total	Incidence [95%CI]
Borghaei H, 2015	3	287	1.05 [–0.13-2.22]
Brahmer J, 2015	1	131	0.76 [–0.73-2.25]
Rizvi NA, 2015	4	117	3.42 [0.13-6.71]
Gettinger S, 2015	3	129	2.33 [–0.28-4.93]
Gettinger S, 2016	1	52	1.92 [–1.81-5.66]
Garon EB, 2015	9	495	1.82 [0.64-3.00]
Herbst RS, 2016	14	682	2.05 [0.99-3.12]
Makoto N, 2015	0	76	0.00 [0.00-0.00]
Makoto N, 2015	0	35	0.00 [0.00-0.00]
Todd MB, 2015	2	807	0.25 [–0.10-0.59]
Reck M, 2016	4	154	2.60 [0.09-5.11]
Socinski MA, 2016	1	267	0.37 [–0.36-1.11]
RE Model			1.15 [0.57-1.73]

B

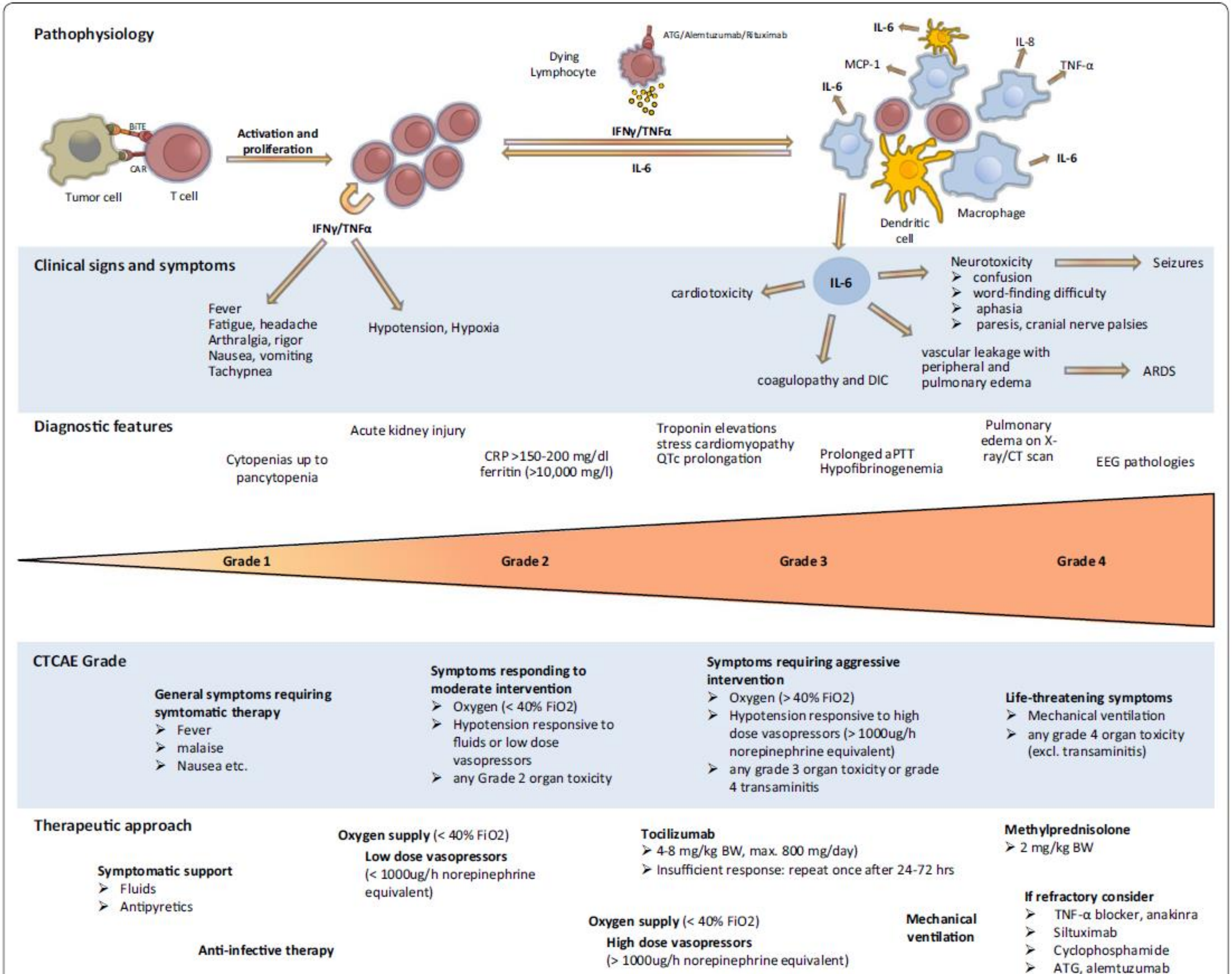
Author, year	3–4 Pneum	Total	Incidence [95%CI]
Besse B, 2015	0	659	0.00 [000-0.00]
Antonia S, 2016	1	59	1.69 [–1.60-4.99]
Spigel DR, 2015	1	137	0.73 [–0.70-2.16]
Herbst RS, 2014	0	53	0.00 [0.00-0.00]
Verschraegen CF, 2016	0	145	0.00 [0.00-0.00]
Fehrenbacher L, 2016	1	144	0.69 [–0.66-2.05]
Rittmeyer A, 2016	4	609	0.66 [0.02-1.30]
RE Model			0.41 [0.00-0.85]

Figure 4 – *Incidence of grade ≥ 3 pneumonitis in studies of programmed death 1 inhibitors (A) and programmed death-ligand 1 inhibitors (B). Pneu = pneumonitis.*

CHEST 2017; 152(2):271-281

Syndrome de fuite capillaire

- atteinte lésionnelle des cellules endothéliales par le traitement anticancéreux : hyperperméabilité capillaire.
- docétaxel, AraC, gemcitabine, conditionnement des greffes de moelle, Il-2,
- Hypotension artérielle, tachycardie, œdèmes, oligurie, insuffisance rénale et détresse respiratoire par œdème pulmonaire.
- oxygénothérapie, support ventilatoire et éventuellement diurétique, corticothérapie (?)
- Si possible, arrêt de l’agent en cause


BiTE
CAR
Tumor cell
T cell
Activation and proliferation
IFNγ/TNFα
Dying Lymphocyte
ATG/Alemtuzumab/Rituximab
IFNγ/TNFα
IL-6
IL-6
MCP-1
IL-8
TNF-α
IL-6
IL-6
Dendritic cell
Macrophage
Grade 1
Grade 2
Grade 3
Grade 4

Pathophysiology

Clinical signs and symptoms

Fever
Fatigue, headache
Arthralgia, rigor
Nausea, vomiting
Tachypnea

Hypotension, Hypoxia

cardiotoxicity

IL-6

coagulopathy and DIC

Neurotoxicity
- confusion
- word-finding difficulty
- aphasia
- paresis, cranial nerve palsies

Seizures

vascular leakage with peripheral and pulmonary edema

ARDS

Diagnostic features

Cytopenias up to pancytopenia

Acute kidney injury

CRP >150-200 mg/dl
ferritin (>10,000 mg/l)

Troponin elevations
stress cardiomyopathy
QTc prolongation

Prolonged aPTT
Hypofibrinogenemia

Pulmonary edema on X-ray/CT scan

EEG pathologies

CTCAE Grade

General symptoms requiring symtomatic therapy
- Fever
- malaise
- Nausea etc.

Symptoms responding to moderate intervention
- Oxygen (< 40% FiO2)
- Hypotension responsive to fluids or low dose vasopressors
- any Grade 2 organ toxicity

Symptoms requiring aggressive intervention
- Oxygen (> 40% FiO2)
- Hypotension responsive to high dose vasopressors (> 1000ug/h norepinephrine equivalent)
- any grade 3 organ toxicity or grade 4 transaminitis

Life-threatening symptoms
- Mechanical ventilation
- any grade 4 organ toxicity (excl. transaminitis)

Therapeutic approach

Symptomatic support
- Fluids
- Antipyretics

Anti-infective therapy

Oxygen supply (< 40% FiO2)
Low dose vasopressors
(< 1000ug/h norepinephrine equivalent)

Tocilizumab
- 4-8 mg/kg BW, max. 800 mg/day)
- Insufficient response: repeat once after 24-72 hrs

Oxygen supply (< 40% FiO2)
High dose vasopressors
(> 1000ug/h norepinephrine equivalent)

Mechanical ventilation

Methylprednisolone
- 2 mg/kg BW

If refractory consider
- TNF-α blocker, anakinra
- Siltuximab
- Cyclophosphamide
- ATG, alemtuzumab

Management of the Critically Ill Adult Chimeric Antigen Receptor-T Cell Therapy Patient: A Critical Care Perspective

Cristina Gutierrez, MD[1]; Colleen McEvoy, MD[2]; Elena Mead, MD[3]; R. Scott Stephens, MD[4]; Laveena Munshi, MD, MSc, FRCPC[5]; Michael E. Detsky, MD[6]; Stephen M. Pastores, MD, FCCM[7]; Joseph L. Nates, MD, MBA, MCCM[8]

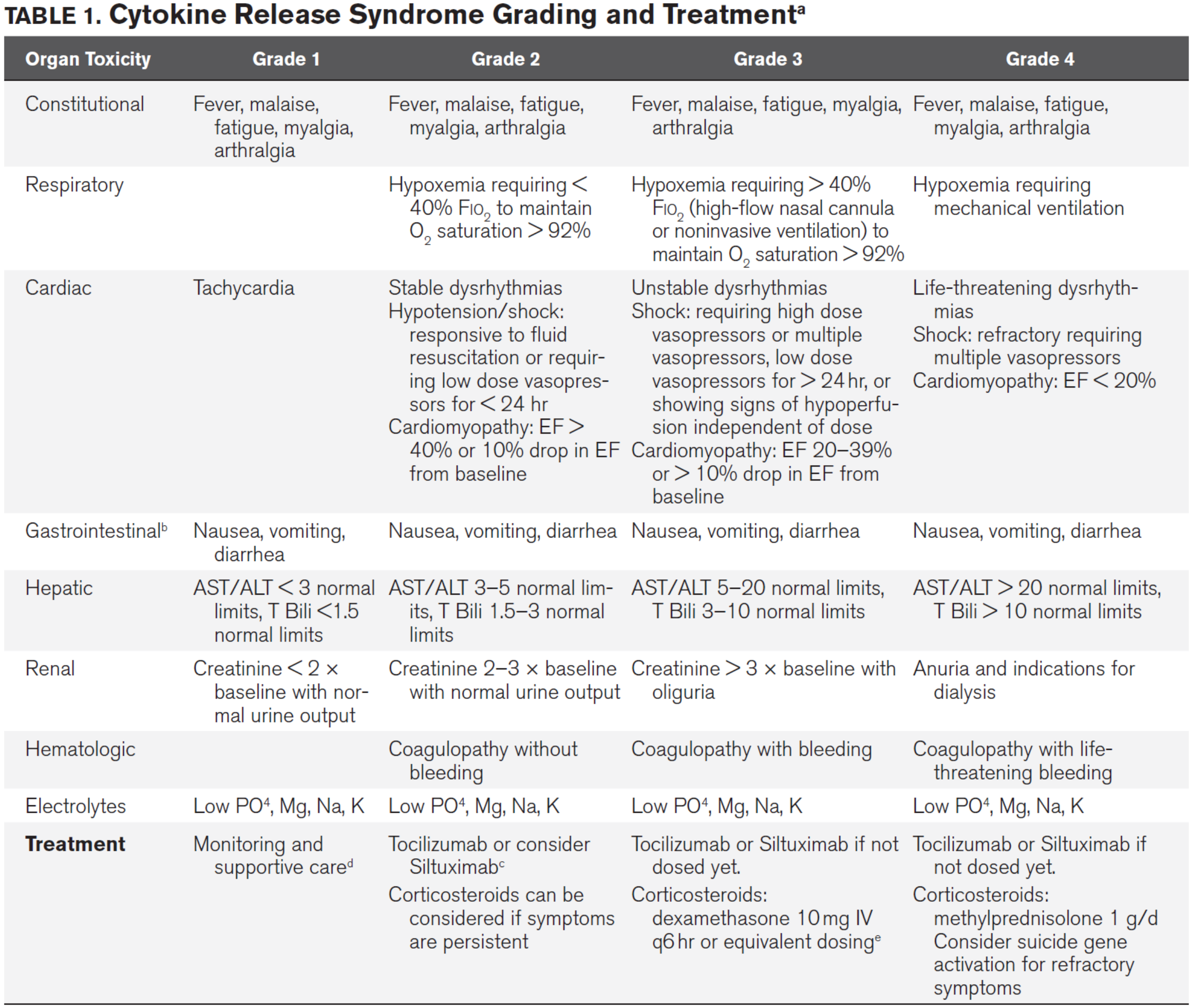


TABLE 1. Cytokine Release Syndrome Grading and Treatment[a]

Organ Toxicity	Grade 1	Grade 2	Grade 3	Grade 4
Constitutional	Fever, malaise, fatigue, myalgia, arthralgia	Fever, malaise, fatigue, myalgia, arthralgia	Fever, malaise, fatigue, myalgia, arthralgia	Fever, malaise, fatigue, myalgia, arthralgia
Respiratory		Hypoxemia requiring < 40% FIO_2 to maintain O_2 saturation > 92%	Hypoxemia requiring > 40% FIO_2 (high-flow nasal cannula or noninvasive ventilation) to maintain O_2 saturation > 92%	Hypoxemia requiring mechanical ventilation
Cardiac	Tachycardia	Stable dysrhythmias Hypotension/shock: responsive to fluid resuscitation or requiring low dose vasopressors for < 24 hr Cardiomyopathy: EF > 40% or 10% drop in EF from baseline	Unstable dysrhythmias Shock: requiring high dose vasopressors or multiple vasopressors, low dose vasopressors for > 24 hr, or showing signs of hypoperfusion independent of dose Cardiomyopathy: EF 20–39% or > 10% drop in EF from baseline	Life-threatening dysrhythmias Shock: refractory requiring multiple vasopressors Cardiomyopathy: EF < 20%
Gastrointestinal[b]	Nausea, vomiting, diarrhea	Nausea, vomiting, diarrhea	Nausea, vomiting, diarrhea	Nausea, vomiting, diarrhea
Hepatic	AST/ALT < 3 normal limits, T Bili <1.5 normal limits	AST/ALT 3–5 normal limits, T Bili 1.5–3 normal limits	AST/ALT 5–20 normal limits, T Bili 3–10 normal limits	AST/ALT > 20 normal limits, T Bili > 10 normal limits
Renal	Creatinine < 2 × baseline with normal urine output	Creatinine 2–3 × baseline with normal urine output	Creatinine > 3 × baseline with oliguria	Anuria and indications for dialysis
Hematologic		Coagulopathy without bleeding	Coagulopathy with bleeding	Coagulopathy with life-threatening bleeding
Electrolytes	Low PO^4, Mg, Na, K	Low PO^4, Mg, Na, K	Low PO^4, Mg, Na, K	Low PO^4, Mg, Na, K
Treatment	Monitoring and supportive care[d]	Tocilizumab or consider Siltuximab[c] Corticosteroids can be considered if symptoms are persistent	Tocilizumab or Siltuximab if not dosed yet. Corticosteroids: dexamethasone 10 mg IV q6 hr or equivalent dosing[e]	Tocilizumab or Siltuximab if not dosed yet. Corticosteroids: methylprednisolone 1 g/d Consider suicide gene activation for refractory symptoms

CCM September 2018 • Volume 46 • Number 9

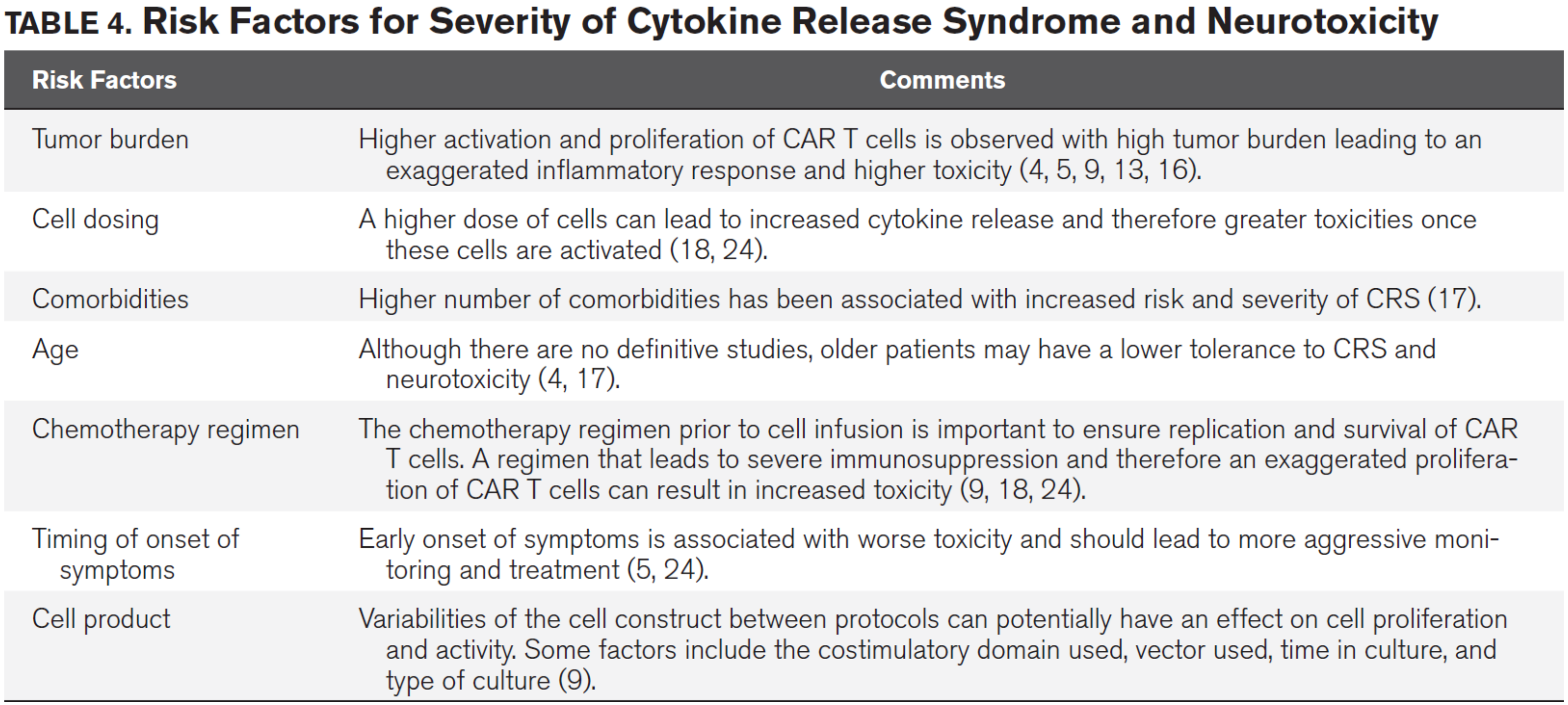


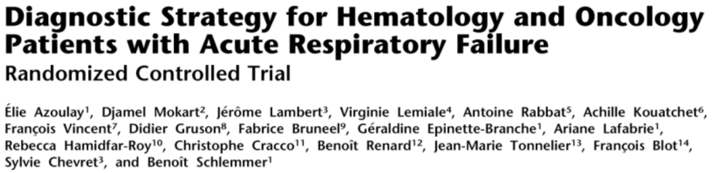
TABLE 4. Risk Factors for Severity of Cytokine Release Syndrome and Neurotoxicity

Risk Factors	Comments
Tumor burden	Higher activation and proliferation of CAR T cells is observed with high tumor burden leading to an exaggerated inflammatory response and higher toxicity (4, 5, 9, 13, 16).
Cell dosing	A higher dose of cells can lead to increased cytokine release and therefore greater toxicities once these cells are activated (18, 24).
Comorbidities	Higher number of comorbidities has been associated with increased risk and severity of CRS (17).
Age	Although there are no definitive studies, older patients may have a lower tolerance to CRS and neurotoxicity (4, 17).
Chemotherapy regimen	The chemotherapy regimen prior to cell infusion is important to ensure replication and survival of CAR T cells. A regimen that leads to severe immunosuppression and therefore an exaggerated proliferation of CAR T cells can result in increased toxicity (9, 18, 24).
Timing of onset of symptoms	Early onset of symptoms is associated with worse toxicity and should lead to more aggressive monitoring and treatment (5, 24).
Cell product	Variabilities of the cell construct between protocols can potentially have an effect on cell proliferation and activity. Some factors include the costimulatory domain used, vector used, time in culture, and type of culture (9).

Syndrome de l'acide rétinoïque

- Agent différentiant
- LA promyélocytaire.
- les cellules leucémiques se différencient, en se divisant, en cellules hématologiques matures.
- 6-27% dans les 2-47 jours du début du TT
- hyperleucocytose, parfois > 50 000/mm³ avec leucostase pulmonaire et défaillance respiratoire, voire SDRA (hémorragie alvéolaire cf coagulopathie)
- support ventilatoire et corticothérapie avec des doses de l'ordre de 2x10 mg de dexa/j
- Mortalité: 3-6% si tt instauré

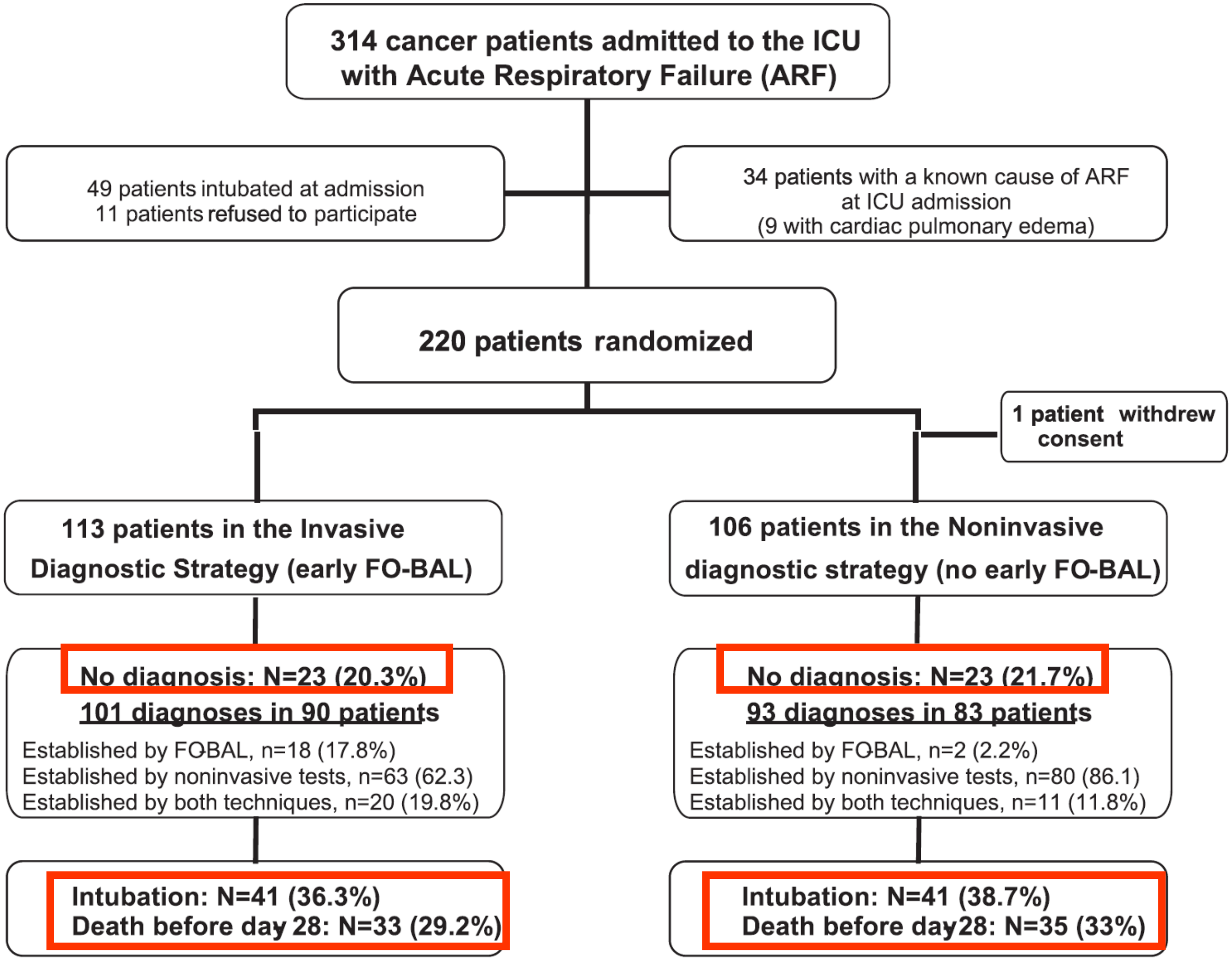
Quel bilan?



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]



314 cancer patients admitted to the ICU with Acute Respiratory Failure (ARF)

49 patients intubated at admission
11 patients refused to participate

34 patients with a known cause of ARF at ICU admission
(9 with cardiac pulmonary edema)

220 patients randomized

1 patient withdrew consent

113 patients in the Invasive Diagnostic Strategy (early FO-BAL)

No diagnosis: N=23 (20.3%)
101 diagnoses in 90 patients
Established by FOBAL, n=18 (17.8%)
Established by noninvasive tests, n=63 (62.3)
Established by both techniques, n=20 (19.8%)

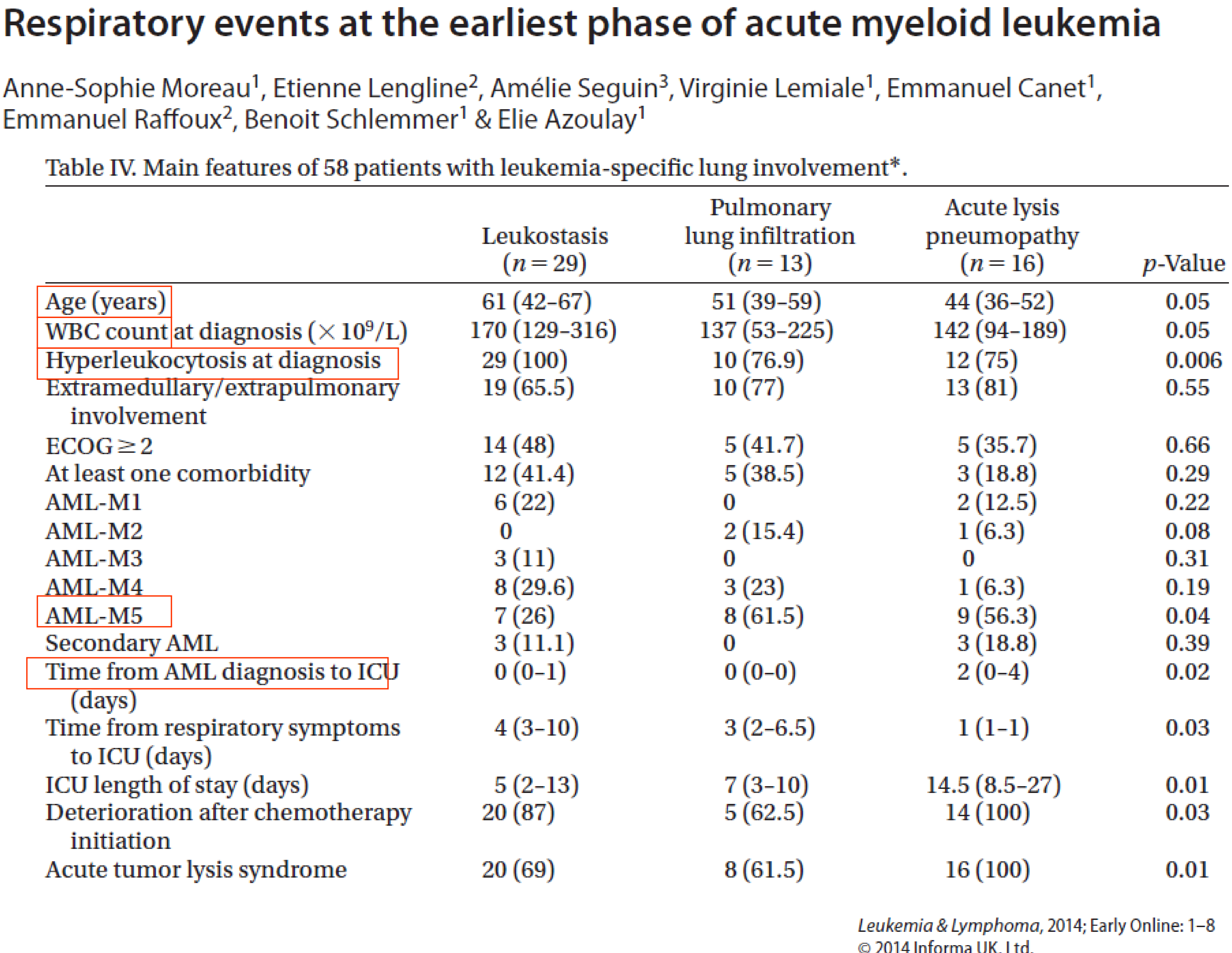
Intubation: N=41 (36.3%)
Death before day 28: N=33 (29.2%)

106 patients in the Noninvasive diagnostic strategy (no early FO-BAL)

No diagnosis: N=23 (21.7%)
93 diagnoses in 83 patients
Established by FOBAL, n=2 (2.2%)
Established by noninvasive tests, n=80 (86.1)
Established by both techniques, n=11 (11.8%)

Intubation: N=41 (38.7%)
Death before day28: N=35 (33%)

Am J Respir Crit Care Med. 2010:1038-46



Respiratory events at the earliest phase of acute myeloid leukemia

Anne-Sophie Moreau[1], Etienne Lengline[2], Amélie Seguin[3], Virginie Lemiale[1], Emmanuel Canet[1], Emmanuel Raffoux[2], Benoit Schlemmer[1] & Elie Azoulay[1]

Table IV. Main features of 58 patients with leukemia-specific lung involvement*.

	Leukostasis ($n = 29$)	Pulmonary lung infiltration ($n = 13$)	Acute lysis pneumopathy ($n = 16$)	p-Value
Age (years)	61 (42–67)	51 (39–59)	44 (36–52)	0.05
WBC count at diagnosis ($\times 10^9$/L)	170 (129–316)	137 (53–225)	142 (94–189)	0.05
Hyperleukocytosis at diagnosis	29 (100)	10 (76.9)	12 (75)	0.006
Extramedullary/extrapulmonary involvement	19 (65.5)	10 (77)	13 (81)	0.55
ECOG ≥ 2	14 (48)	5 (41.7)	5 (35.7)	0.66
At least one comorbidity	12 (41.4)	5 (38.5)	3 (18.8)	0.29
AML-M1	6 (22)	0	2 (12.5)	0.22
AML-M2	0	2 (15.4)	1 (6.3)	0.08
AML-M3	3 (11)	0	0	0.31
AML-M4	8 (29.6)	3 (23)	1 (6.3)	0.19
AML-M5	7 (26)	8 (61.5)	9 (56.3)	0.04
Secondary AML	3 (11.1)	0	3 (18.8)	0.39
Time from AML diagnosis to ICU (days)	0 (0–1)	0 (0–0)	2 (0–4)	0.02
Time from respiratory symptoms to ICU (days)	4 (3–10)	3 (2–6.5)	1 (1–1)	0.03
ICU length of stay (days)	5 (2–13)	7 (3–10)	14.5 (8.5–27)	0.01
Deterioration after chemotherapy initiation	20 (87)	5 (62.5)	14 (100)	0.03
Acute tumor lysis syndrome	20 (69)	8 (61.5)	16 (100)	0.01

Leukemia & Lymphoma, 2014; Early Online: 1–8

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

Complications pulmonaires non infectieuses des maladies myéloprolifératives et des syndromes myélodysplasiques

C. Lamour[1], A. Bergeron[2]

Tableau III.
Mécanismes physiopathologiques selon la présentation clinique.

Présentation radioclinique	Étiologies ou pathologies associées	Éléments utiles au diagnostic
Aspect de syndrome tumoral	Hématopoïèse extramédullaire Chloromes	Scintigraphie pulmonaire au technétium 99 Scanner Ponction, biopsie
Pneumopathie infiltrante	Hématopoïèse extramédullaire Syndrome paranéoplasique auto-immun Syndrome de Sweet Syndrome hyperéosinophilique Protéinose alvéolaire Pneumonie organisée	Scanner thoracique Scintigraphie au technétium LBA Ponction, biopsie
Épanchements pleuraux et péricardiques	Infiltration tumorale Hématopoïèse extramédullaire Chloromes Mécanismes immunitaires	Ponction pleurale, Biopsie
HTAP	Association avec les SMP	Échographie cardiaque Cathétérisme cardiaque

Rev Mal Respir 2009 ; 26 : 655-65

Pneumopathie à *Pneumocystis*

- Hémopathie maligne (greffe de moelle allogénique) mais pas exceptionnelle en cas de tumeur solide (corticoïdes, paclitaxel).
- Mortalité 30 %.
- Fièvre, pneumopathie diffuse avec atteinte interstitielle puis alvéolaire, SDRA (choc rare.)
- LBA (coloration argentique ou d'une technique immunocytologique ou par biologie moléculaire).
- Triméthoprine-sulfaméthoxazole (cotrimoxazole) deux semaines (respectivement à raison de 20 et 100 mg/kg/j) ou pentamidine IV + corticoïdes (1à 4x 60 mg/j de prednisone)

PNEUMONIE À CMV

- Greffe de moelle osseuse allogénique
- Les trois premiers mois suivant la transplantation
- Pneumopathie interstitielle diffuse, avec hypoxémie et installation d'une dépression médullaire, SDRA.
- Isolement du virus dans le sang ou au LBA (ou biopsie pulmonaire).
- Ganciclovir et hautes doses d'immunoglobulines anti-CMV
- Mortalité supérieure à 80 %

ASPERGILLOSE PULMONAIRE

- Neutropénie prolongée, corticothérapie et/ou greffe de moelle
- Fièvre résistant aux antibiotiques antibactériens, toux, douleurs pleurale et dyspnée.
- Images nodulaires ou infiltratives diffuses pouvant être excavées avec un signe du halo ou du grelot
- Filaments mycéliens à l’examen direct et de l’aspergillus à la culture de l’aspiration trachéale ou LBA
- Localisations extrapulmonaires (cérébrales)
- Prévention
- Traitement

INSTITUT
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INSTITUUT

ULB iris

SYNDROME DE LEUCOSTASE

- LAM 4 et 5
- hyperleucocytose (> 100 000/mm3)
- Agrégation des blastes dans la microcirculation, thrombus intravasculaire
- Hyperviscosité sanguine
- détresse respiratoire, SDRA , encéphalopathie.
- Oxygénothérapie, support ventilatoire, leucaphérèses, chimiothérapie.

Characteristics and outcomes of cancer patients requiring mechanical ventilatory support for >24 hrs*

Márcio Soares, MD, PhD; Jorge I. F. Salluh, MD; Nelson Spector, MD, PhD; José R. Rocco, MD, PhD

Table 2. Characteristics related to the underlying malignancy (n = 463)

Variable	No. (%)
Type of cancer	
Solid tumor	359 (78)
Head and neck cancer	68 (15)
Lower gastrointestinal cancer	60 (13)
Brain tumor	57 (12)
Upper gastrointestinal cancer	52 (11)
Lung cancer	45 (10)
Breast cancer	25 (5)
Urogenital cancer	24 (5)
Other	28 (6)
Hematologic malignancies	104 (22)
Non-Hodgkin's lymphoma	57 (12)
Leukemia	21 (5)
Multiple myeloma	14 (3)
Hodgkin's disease	9 (2)
Other	3 (1)
Extent (solid tumors only)	
Locoregional	271 (75)
Metastatic	88 (25)
Cancer status	
Controlled	228 (49)
Newly diagnosed	105 (23)
Recurrence/progression	130 (28)
Performance status	
0–1 (ambulant)	246 (53)
2 (minor assistance)	71 (15)
3–4 (major assistance/bedridden)	146 (32)
Leukopenia	35 (8)
Anticancer treatments (previous 6 mos)[a]	
Chemotherapy	161 (35)
Surgery with curative intent	152 (33)
Radiation therapy	136 (29)
None	56 (12)

Crit Care Med 2005 Vol. 33, No. 3

Table 3. Main reasons for mechanical ventilatory support (n = 463)[a]

Reasons for Mechanical Ventilatory Support[a]	No. (%)
Sepsis	291 (63)
Pulmonary	140 (30)
Nonpulmonary	151 (33)
Intraabdominal infection	77 (17)
Urinary tract infection	13 (3)
Soft tissue/skin	8 (2)
Central nervous system	5 (1)
Other/unknown	48 (10)
ARDS	189 (41)
Coma	71 (15)
Airway/pulmonary involvement by the tumor	53 (11)
Pulmonary embolism	32 (7)
Cardiopulmonary arrest	29 (6)
Nonseptic shock	15 (3)
Cardiogenic pulmonary edema	14 (3)
Hemoptysis/alveolar hemorrhage	12 (3)
Aspiration	8 (2)
Hypertensive pneumothorax	6 (1)
Acute exacerbation of COPD	4 (1)
Miscellaneous/unknown	30 (6)

Table 5. Multivariable analysis of factors associated with hospital mortality (n = 463)

Variable	Coefficient ± SE	Odds Ratio (95% CI)	p Value
Age, yrs			
<40		1.00	—
40–70	1.128 ± 0.333	3.09 (1.61–5.93)	.001
>70	2.225 ± 0.408	9.26 (4.16–20.58)	<.001
Performance status			
0–1 (ambulant)		1.00	—
2 (minor assistance)	0.367 ± 0.347	1.44 (0.73–2.85)	.291
3–4 (major assistance/bedridden)	0.920 ± 0.299	2.51 (1.40–4.51)	.002
Cancer status			
Controlled		1.00	—
Newly diagnosed	0.220 ± 0.304	1.25 (0.69–2.26)	.496
Recurrence/progression	1.233 ± 0.328	3.43 (1.81–6.53)	<.001
$\mathrm{PaO_2/FIO_2}$ ratio			
≥300		1.00	—
150–299	−0.327 ± 0.268	0.72 (0.43–1.21)	.218
<150	0.973 ± 0.323	2.64 (1.40–4.99)	.003
SOFA excluding respiratory points (each 4 points change)	0.852 ± 0.165	2.34 (1.70–3.24)	<.001
Airway/pulmonary involvement by the tumor as reason for MV	1.745 ± 0.558	5.73 (1.92–17.08)	.002
Constant	−2.199		

TABLE 3 Univariate analysis of associations between DIRECT criteria and aetiological groups of acute respiratory failure in cancer patients

Characteristics	Study cohort	Bacterial pneumonia	Opportunistic pulmonary infections	Noninfectious lung disorders	p-value
Subjects n	424	201	131	92	
Delay					
Delay since onset of malignancy or HSCT days	237 (52–1023)	384 (62–1428)	225 (68–830)	167 (24–495)	0.0063
Delay since onset of symptoms days	3 (1–6)	2 (1–5)	4 (1–8)	2 (1–6)	0.0034
Patterns of immune deficiency					
Lymphoproliferative disorder	141 (33)	65 (32)	51 (39)	25 (27)	0.091
Acute leukaemia	110 (26)	41 (20)	35 (27)	34 (37)	0.012
Multiple myeloma	48 (11)	36 (18)	6 (5)	6 (7)	0.195
Allogeneic HSCT	60 (14)	25 (12)	25 (19)	10 (11)	0.15
Solid tumours	65 (15)	34 (17)	14 (11)	17 (19)	0.18
Neutropenia	149 (35)	71 (35)	48 (37)	30 (33)	0.82
Steroids	193 (46)	93 (46)	68 (52)	32 (35)	0.031
Radiographic appearance					
Cardiomegaly	262 (62)	124 (62)	80 (61)	58 (63)	0.80
Unilateral pattern	94 (22)	75 (37)	15 (12)	4 (4)	<0.0001
Interstitial	139 (33)	69 (34)	41 (31)	29 (32)	0.77
Alveolar	246 (58)	116 (58)	80 (61)	50 (54)	0.62
Pleural effusion	102 (24)	48 (24)	25 (19)	29 (32)	0.11
Clinical picture					
Bronchial breathing	24 (6)	18 (9)	3 (2)	3 (3)	0.016
Bilateral crackles	149 (35)	49 (24)	61 (47)	39 (42)	<0.0001
Unilateral crackles	112 (26)	73 (36)	21 (16)	18 (20)	<0.0001
Shock at admission	144 (34)	85 (42)	37 (28)	22 (24)	0.002
Findings by HRCT					
Nodules	113 (26)	62 (31)	33 (25)	18 (12)	0.35
Ground-glass opacity	237 (56)	103 (51)	84 (64)	50 (54)	0.23
Consolidation	300 (70)	156 (78)	84 (64)	60 (65)	0.09
Septal lines	101 (24)	40 (20)	29 (22)	32 (35)	0.11
Halo signs	29 (7)	18 (9)	10 (8)	1 (2)	0.18

TABLE 4. INFECTIONS DIAGNOSED BY NONINVASIVE TESTS

Test/Infections	Actually Performed*	Positive Test	Diagnostic Test[†]
1. Imaging studies		Not sufficient for diagnosing pulmonary infections	
Chest radiograph	219		
High-resolution computed tomography	191		
2. Echocardiography	191	For diagnosing cardiogenic ulmonary edema only	
3. Sputum examination for			
Bacteria	194	39	34
Candida spp.	193	8	0
Other fungi	193	8	6
Tuberculosis	193	1	1
4. Induced sputum (*P. jiroveci*)	148	10	10
5. Nasopharyngeal aspirates	190	18	16
6. Blood cultures	219	27	25
7. Polymerase chain reaction test for			
Herpes viridae	184	9	3
Cytomegalovirus	219	10	3
8. Circulating *Aspergillus* galactomanan	219	11	11
9. Serologic tests for			
Chlamydiae pneumoniae	203	1	1
Mycoplasma pneumoniae	203	2	2
Legionella pneumophila	203	3	3
10. Urine antigen for			
Legionella pneumophila	214	1	1
Streptococcus pneumoniae	214	5	5

TABLE 2. CAUSES OF ACUTE RESPIRATORY FAILURE IN THE TWO DIAGNOSTIC-STRATEGY GROUPS

Cause	Routine Day 1 FO-BAL, N = 113 (%)	N (%) Diagnosed by BAL	± Day 3 FO-BAL, N = 106 (%)	N (%) diagnosed by BAL
Bacterial pneumonia	47 (41.6)		39 (36.8)	
Microbiologically documented	32 (68)	17 (36.2)	27 (70)	4 (10.2)
Clinically documented	15 (32)	—	12 (30)	—
Viral pneumonia	7 (6.2)	6 (86)	19 (17.9)	10 (55.5)
Invasive yeast and mold infections	14 (12.4)	7 (50)	9 (8.5)	3 (33.3)
Including invasive pulmonary aspergillosis only	10 (8.8)	6 (60)	8 (7.5)	3 (37)
Pneumocystis pneumonia*	9 (8)	9 (100)	10 (9.4)	1 (10)
Pulmonary infiltration by the malignancy	10 (8.8)	3 (30)	6 (5.7)	0
Cardiogenic pulmonary edema	7 (6.2)	0	3 (2.8)	0
Respiratory failure during neutropenia recovery	2 (1.8)	0	1 (0.9)	0
Pulmonary toxoplasmosis	1 (0.9)	1 (100)	1 (0.9)	0
Pulmonary tuberculosis	0		1 (0.9)	0
Cryptogenic organizing pneumonia	1 (0.9)	0	1 (0.9)	0
Idiopathic alveolar hemorrhage	1 (0.9)	1 (100)	0	
Miscellaneous[†]	2 (1.8)	0	3 (2.8)	0
Total number of identified causes	101		93	
Patients with two identified causes	7 (6.2)		8 (7.5)	
Patients with three identified causes	2 (1.8)		1 (0.9)	
No identified cause	23 (20.3)		23 (21.7)	

TABLE 3. OUTCOMES AND ICU MANAGEMENT IN THE TWO DIAGNOSTIC-STRATEGY GROUPS

	Routine Day 1 FO-BAL (*n* = *113*)	Noninvasive Group (*n* = *106*)	
Primary end point			*P* Value
Need for endotracheal mechanical ventilation, pts	40	41	0.68
Estimated rate (95% CI)	35.4% (26.6–45)	38.7% (29.4–48.7)	OR = 0.87 (0.50–1.50) Adjusted OR* = 1.11 (0.58–2.11); *P* = 0.76
Major secondary end point			
Number of patients with no identified diagnosis	23	23	Between-group risk difference (90% CI),%
Estimated rate (95% CI)	20.4% (13.4–29)	21.7% (14.3–30.8)	−1.3 (−10.4 to 7.7)
Other secondary end points			*P* value
Day 28 deaths	33	35	
Estimated rate (95% CI)	29.2% (21–38.5)	33% (24.2–42.8)	0.56
Median number of antibiotic-free days (Q1–Q3)	2 (0–2)	2 (0–3)	0.78
ICU-acquired infections	9	13	
Estimated rate (95% CI)	8% (3.7–14.6)	12.2% (6.7–20.1)	0.37
Acquisition of multiresistant bacteria	6	10	
Estimated rate (95% CI)	25.3% (2–11.2)	9.4% (4.6–16.7)	0.30

COMPLICATIONS DES GREFFES DE MOELLE OSSEUSE

- infections pulmonaires
- hémorragie alvéolaire
- syndrome de fuite capillaire
- toxicités médicamenteuses
- pneumopathie interstitielle idiopathique
- bronchiolite oblitérante avec trouble ventilatoire obstructif
- maladie veino-occlusive pulmonaire.

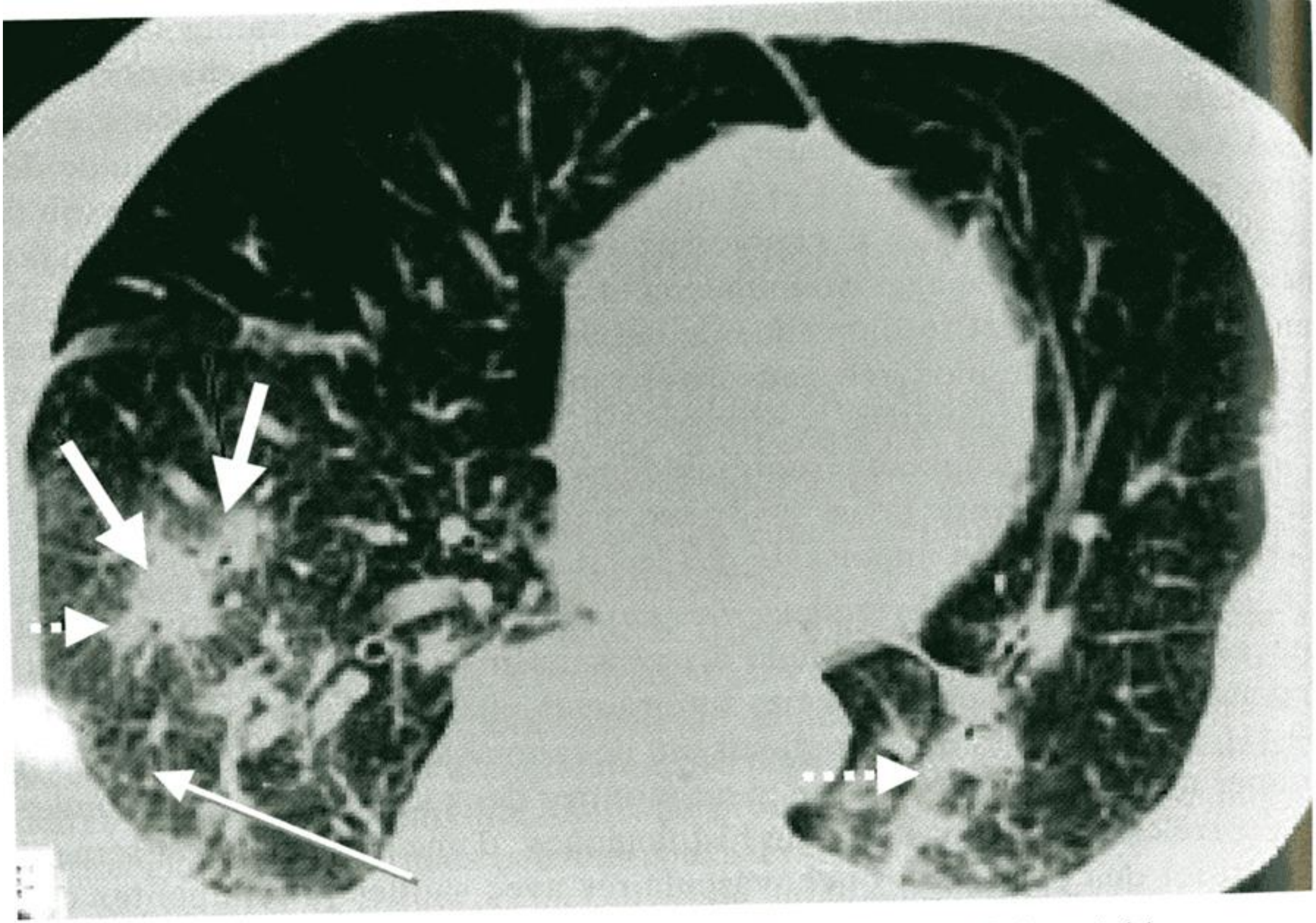


Fig. 4. Infiltration tumorale leucémique : opacités en verre dépoli (flèche ombrée), épaississement des paquets bronchovasculaires (flèches pointillés), proéminence des artères pulmonaires périphériques et multiples nodules (flèches pleines).

51 ans
CBNPC traité par radiochimiotéhrapie
6 mois après: toux, dyspnée, perte de poids

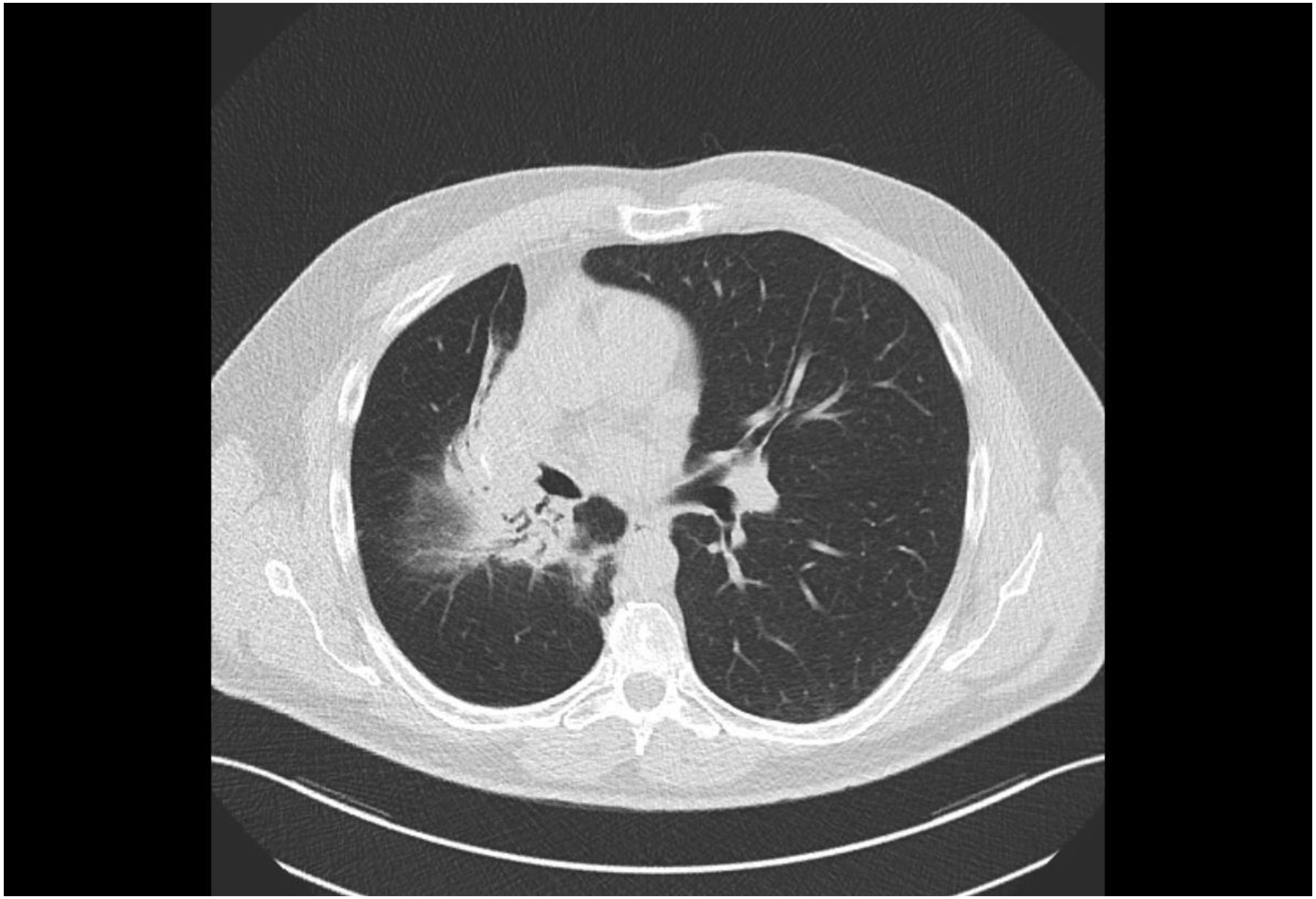
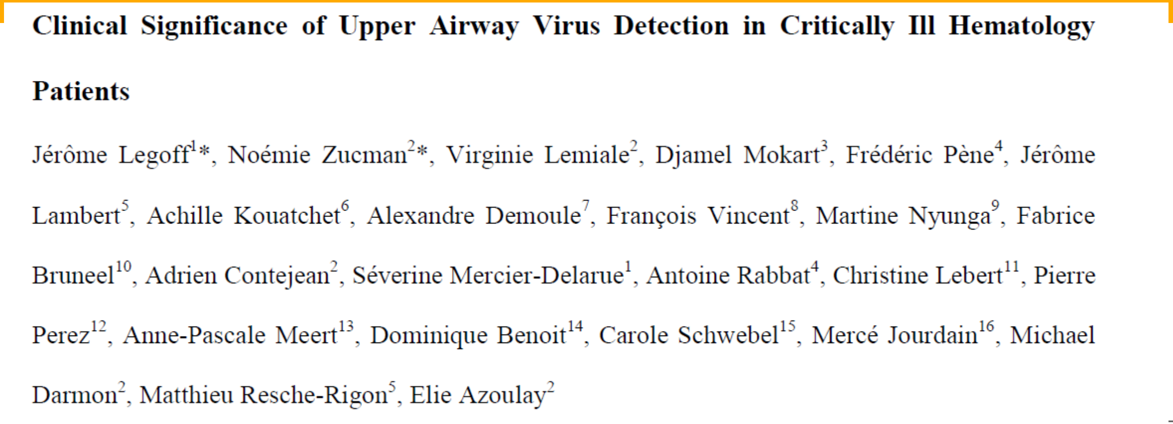


Table 2 Cohort characteristics and outcomes

	All patients $N = 14$	Survivors $n = 7$	Nonsurvivors $n = 7$	P value
Characteristics at ICU admission				
Age	32 (22–51)	23 (21–44)	48 (30–58)	0.14
Male sex	8	4	4	1.00
CCI	2 (2–2)	2 (2–2)	2 (2–4)	0.48
SAPS II	51 (42–65)	56 (43–63)	45 (39–68)	0.90
Prior allogeneic stem cell transplantation	4	0	4	<0.01
Days from diagnosis of HM to ECMO	87 (6–907)	0 ((–1)–116)	759 (69–1,228)	0.04
Days from ICU admission to ECMO	2 (0–3)	1 (0–2)	3 (1–11)	0.08
Days from intubation to ECMO	2 (1–5)	1 (0–2)	3 (1–9)	0.17
Characteristics at ECMO baseline				
SOFA score	12 (11–13)	12 (12–19)	12 (11–15)	0.79
Lung injury score	3.3 (3.3–3.7)	3.3 (2.3–3.7)	3.5 (3.3–3.8)	0.09
PaO_2/FiO_2 ratio	60 (53–65)	63 (51–106)	60 (48–61)	0.44
pH	7.29 (7.23–7.37)	7.29 (7.23–7.39)	7.37 (7.21–7.46)	0.52
$PaCO_2$, mm Hg	49 (43–59)	41 (38–49)	55 (48–72)	0.05
Lactate, m*M*	2.2 (1.6–4.8)	3.8 (1.6–7.1)	2.0 (1.0–5.0)	0.34
Hemoglobin, g/dl	9.4 (8.8–10.4)	9.4 (8.6–10.5)	9.8 (8.4–10.4)	0.90
Leukocytes, G/L	6.0 (2.5–12.6)	11.0 (3.6–17.0)	5.6 (2.0–12.8)	0.34
Platelets, G/L	38 (30–113)	64 (29–201)	35 (10–88)	0.21
Prothrombin time, %	70 (43–74)	50 (18–72)	73 (64–78)	0.22
Fibrinogen, mg/dl	436 (220–522)	473 (160–627)	421 (294–531)	1.00
Etiology of ARF determined[a]	7	5	2	0.29
Clinical diagnosis of pneumonia	10	3	7	0.07
Characteristics during ECMO				
Venoarterial ECMO	3	3	0	0.19
Duration of ECMO therapy, days	8.5 (4–16)	4 (3–9)	10 (7–28)	0.08
Diagnosis of HM on ECMO	4	4	0	0.07
Chemotherapy on ECMO	5	4	1	0.27
Vasopressors	14	7	7	na
Hemofiltration	5	2	3	1.00
Major bleeding events	5	1	4	0.27
Number of packed red blood cell units	8 (4–14)	4 (3–8)	14 (6–27)	0.02
Number of platelet concentrates	5 (1–17)	2 (0–5)	23 (14–26)	0.01
Outcome				
ICU LOS, days	22 (14–42)	22 (21–77)	18 (11–40)	0.12
Hospital LOS, days	56 (44–101)	63 (49–110)	45 (15–133)	0.46
ICU and hospital survival, *n* (%)	7 (50%)			

Table 1. Characteristics of the malignancy

Patients	Early Decedents (n = 85)	Decedents After Day 4 (n = 62)	Hospital Survivors (n = 41)	*p* Value
Age, yrs (IQR)	51 (36–67)	56.8 (47.2–66.7)	44.7 (42.1–58.8)	.05
Male gender, n (%)	55 (64)	43 (69.3)	26 (63.4)	.6
Comorbidities, n (%)				
Hypertension	30 (35.3)	19 (30.6)	5 (12.1)	.03
COPD	8 (9.4)	7 (11.3)	6 (14.6)	.7
Chronic heart failure	4 (4.7)	3 (4.8)	2 (4.8)	.9
Long term steroids	1 (1.2)	3 (4.8)	3 (7.3)	.6
One comorbidity	29 (34.1)	35 (56.4)	19 (46.3)	.4
Chronic health status, n (%)				
Normal or slight alteration	74 (87.1)	49 (78.9)	32 (78)	.7
Altered	11 (12.9)	13 (20.9)	9 (21.9)	.9
Bedridden	0	0	0	—
Characteristics of the malignancy, n (%)				
Acute leukemia	25 (29.4)	20 (32.3)	11 (26.8)	.5
Chronic lymphocytic leukemia	5 (6)	3 (4.8)	2 (4.9)	.9
Non-Hodgkin's lymphoma	20 (23.5)	14 (22.6)	11 (26.8)	.6
Multiple myeloma	10 (11.8)	7 (11.3)	4 (9.7)	.8
Lung and breast cancer	12 (14.1)	8 (12.9)	6 (15.3)	.8
Other solid tumor	13 (15.3)	10 (16.1)	7 (17)	.9
Time from diagnosis, days (IQR)	54 (11–179)	37 (6–340)	67 (15–343)	.8
Treatments received for the malignancy				
Courses of chemotherapy, n (IQR)	3 (1–3)	2.5 (0–4)	3.3 (0–5.25)	.7
Autologous stem cell transplantation, n (%)	10 (11.7)	9 (14.5)	5 (12.9)	.8
Status of the malignancy at ICU admission, n (%)				
First 3 months of the treatment	45 (52.9)	36 (58)	23 (56)	.4
Remission or stability	40 (47.1)	21 (34)	16 (39)	.6
Relapse	0	4 (6.5)	2 (5)	.2



Clinical Significance of Upper Airway Virus Detection in Critically Ill Hematology Patients

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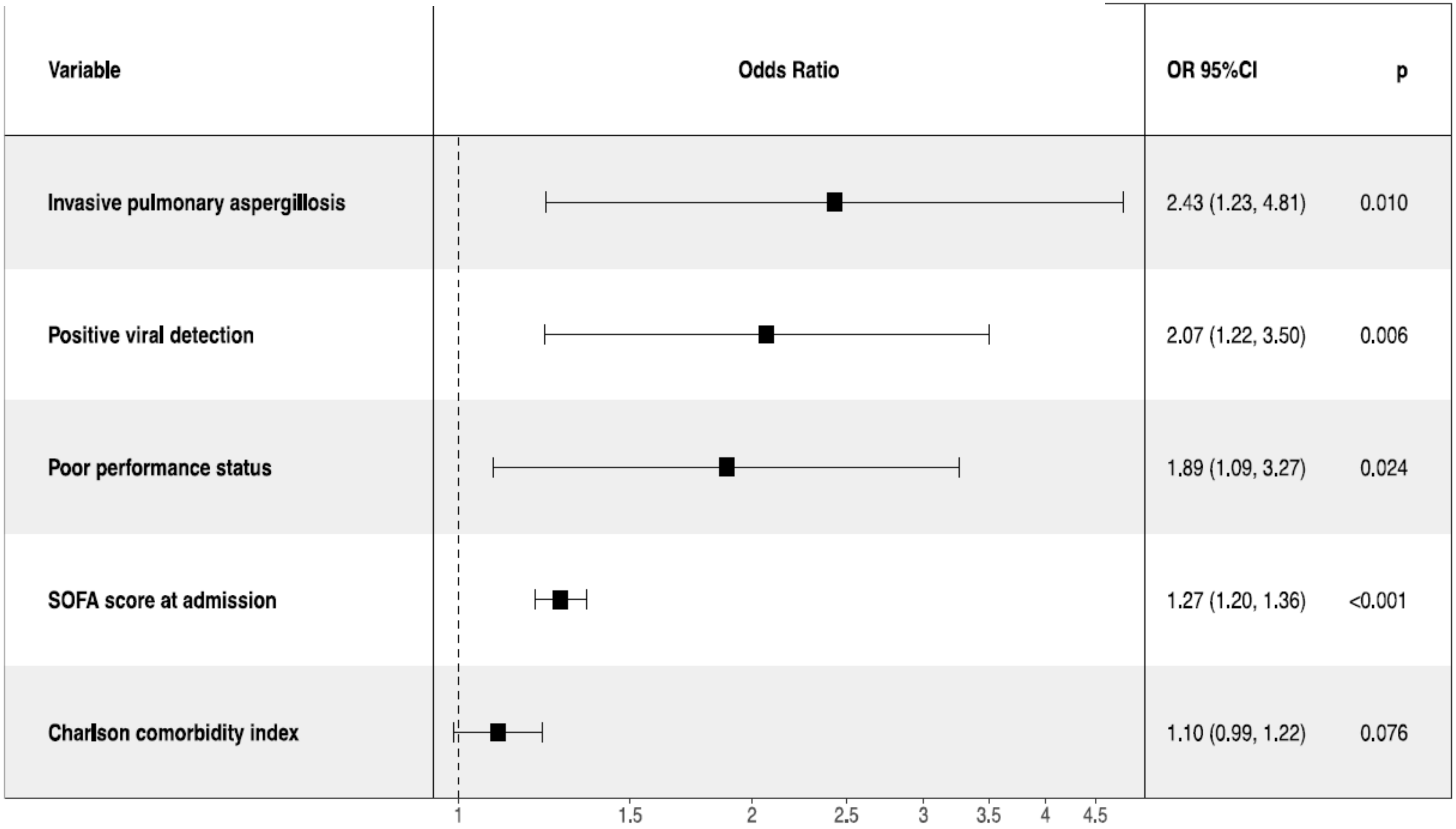
747 patients
447 with ARF
21.3% positive
56.4% rhino/enterovirus
30.7% (para)influenza//RSV



Variable	OR 95%CI	p
Invasive pulmonary aspergillosis	2.43 (1.23, 4.81)	0.010
Positive viral detection	2.07 (1.22, 3.50)	0.006
Poor performance status	1.89 (1.09, 3.27)	0.024
SOFA score at admission	1.27 (1.20, 1.36)	<0.001
Charlson comorbidity index	1.10 (0.99, 1.22)	0.076

AJRCCM Articles in Press. Published on 19-September-2018