





Faut-il isoler les patients neutropeniques



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Conflits d'intérêts

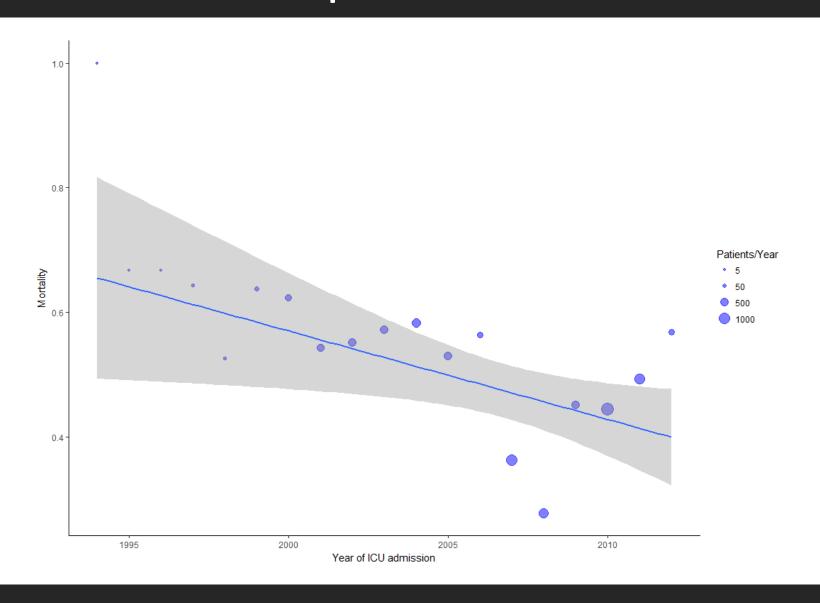
Research grants: MSD, Astute medical

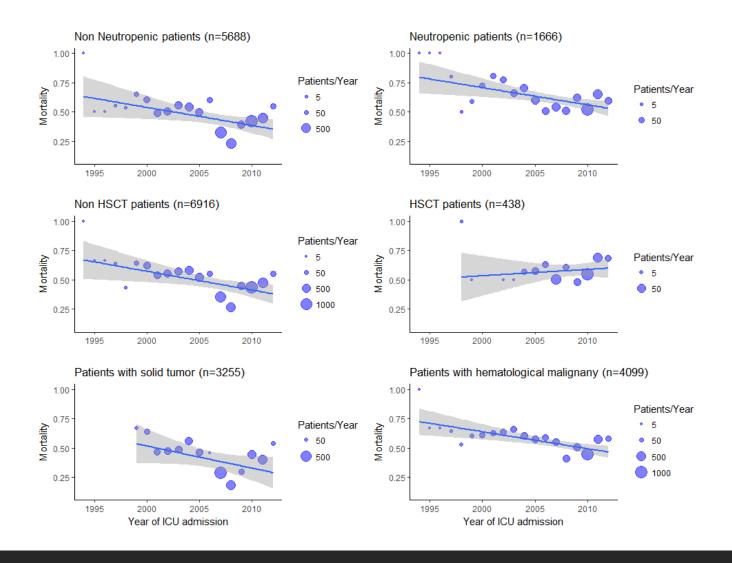
Speaker fees: MSD, Astellas, Bristol Myers Squibb, Gilead

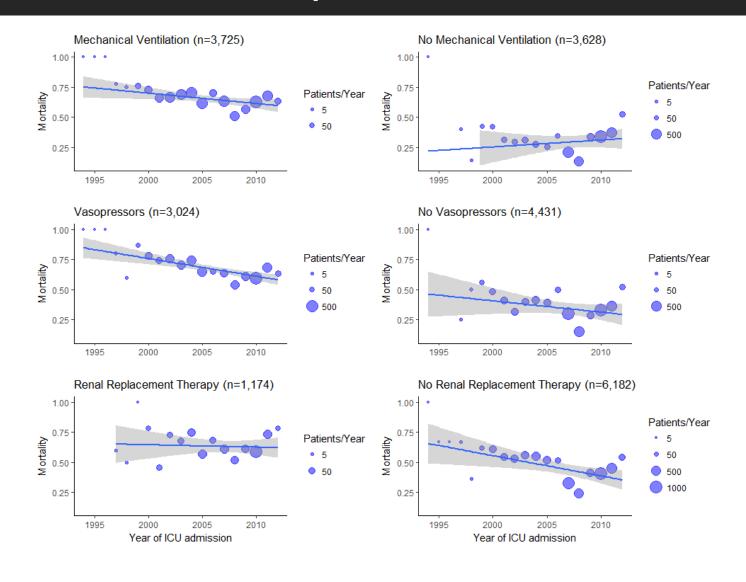
Support in organizing educational meetings: MSD, Astellas, JazzPharma

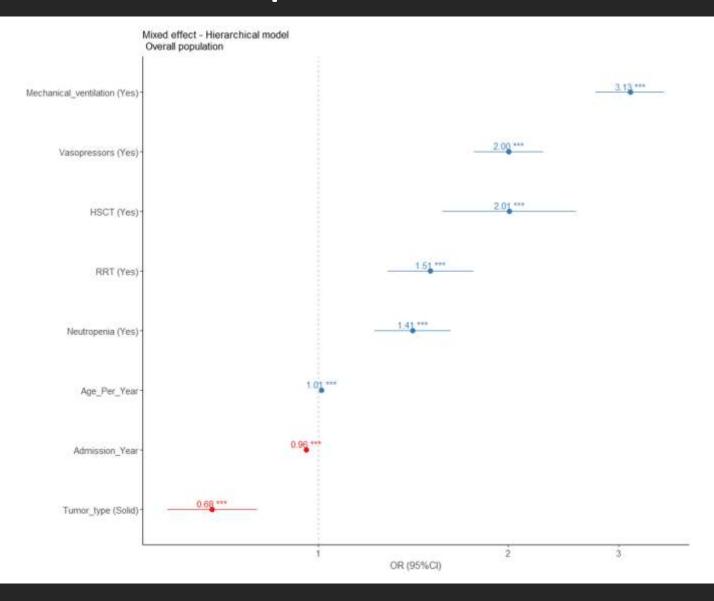
Advisory board: Sanofi Aventis, Gilead-Kite

- Coordination des RFE SRLF sur la gestion de la neutropénie en réanimation
- Investigateur coordonnateur de l'étude Combination-Lock









Repenser les prises en charge

• Antibiothérapie dans l'heure

Monocentre cohort study (Institut Paoli Calmette)

118 Neutropenic patients with severe sepsis/septic shock

Table 1 M	Iultivariate anal	ysis of independent	factors associated wi	th ICU mortality
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Odds ratio	95 % confidence interval	p
1 6.4 0.7 1.4 4.8	Reference 1.6–26 0.2–2.5 1.2–1.6 1.3–18 2.5–33	0.01 0.63 <0.001 0.02 0.002
	1 6.4 0.7 1.4 4.8	1 Reference 6.4 1.6–26 0.7 0.2–2.5 1.4 1.2–1.6 4.8 1.3–18

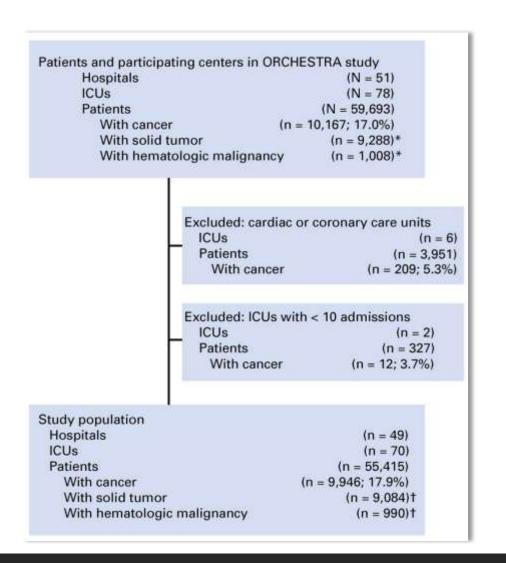
ICU intensive care unit, SOFA sequential organ failure assessment

- Antibiothérapie dans l'heure
- Admission précoce

• Influence of early ICU admission on mortality in Critically III Cancer Patients

	Experim				Weight	Weight		Risk Ratio
Study	Events	Total	Events	Total	(fixed)	(random)	MH, Fixed + Random, 95% CI	MH, Fixed + Random, 95% CI
Azoulay, 2013	144	451	241	560	37.8%	17.4%	0.74 [0.63, 0.88]	-
Bird, 2012	41	107	50	92	9.5%	15.1%	0.71 [0.52, 0.96]	-
Doukhan, 2017	193	246	38	54	11.0%	17.1%	1.11 [0.93, 1.34]	 ■
Lee, 2015	64	221	168	304	24.9%	16.4%	0.52 [0.42, 0.66]	
lengline, 2012	10	42	7	20	1.7%	7.1%	0.68 [0.30, 1.52]	++-
Song , 2012	32	100	72	99	12.7%	15.0%	0.44 [0.32, 0.60]	
Thiery, 2005	48	105	8	13	2.5%	11.8%	0.74 [0.46, 1.20]	
Total (fixed effect, 95% CI)		1272		1142	100.0%		0.69 [0.62, 0.76]	+
Total (random effects, 95% C	I)					100.0%	0.69 [0.52, 0.90]	
Heterogeneity: Tau ² = 0.10; Chi ² =	40.64, df =	6 (P <	: 0.01); I ² :	= 85%				
Test for overall effect (fixed effect)	: Z = -7́.56 (P < 0.0	01)					0.5 1 2
Test for overall effect (random effe	ects): Z = -2.	.72 (P	< 0.01)					

- Antibiothérapie dans l'heure
- Admission précoce
- Contacts étroits avec l'oncologue ou l'hématologue



Variables associated with mortality

Center level		
Type of hospital		
General	1.000	
Referral cancer center	1.210 (0.893 to 1.638)	.217
Training programs in critical care in ICU		
No	1.000	
Yes	1.376 (1.048 to 1.808)	.021
Presence of clinical pharmacist in ICU		
No	1.000	
Yes	0.666 (0.492 to 0.900)	.008
Daily meetings between oncologists and		
intensivists for care planning in all patients		
No	1.000	
Yes	0.688 (0.520 to 0.910)	.009
Implemented clinical protocols†	0.923 (0.865 to 0.984)	.015

- Antibiothérapie dans l'heure
- Admission précoce
- Contacts étroits avec l'oncologue ou l'hématologue
- Enlever le cathéter si pas de point d'appel infectieux

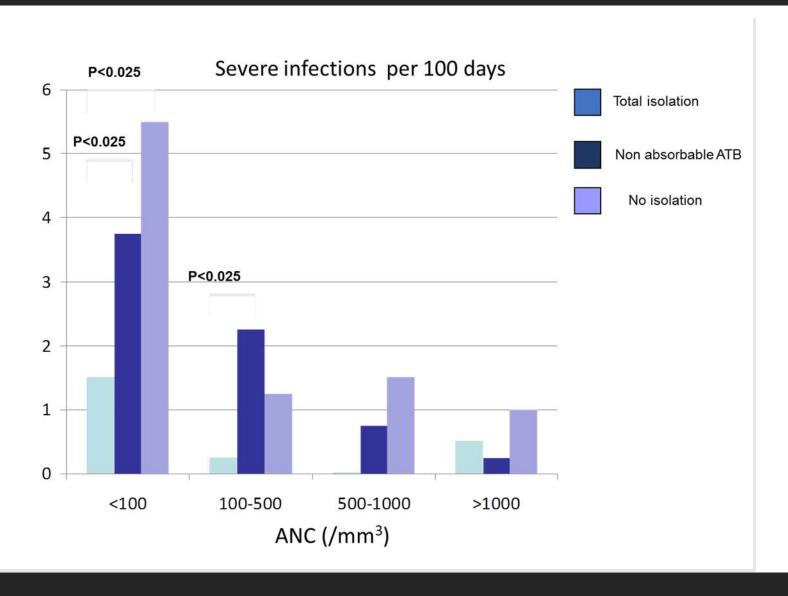
Variable, N (%) or Median (25th–75th)	Alive $(n = 215)$	Dead $(n = 213)$	Odds Ratio (95% Confidence Interval)	p
Age, yrs	47 (35–57)	54 (43-65)	1.036 (1.02-1.05)	<.0001
Intensive care unit admission during the second period (between 2004 and 2008)	139 (64.6)	105 (49.3)	0.56 (0.36–0.89)	.01
Shock	123 (57.2)	181 (85.0)	2.69 (1.65-4.38)	<.0001
Acute respiratory failure	61 (28.4)	171 (80.3)	1.98 (1.14-3.44)	.015
Neurologic failure	7 (3.2)	37 (17.4)	4.03 (1.03-15.8)	.04
Hepatic failure	7 (3.2)	20 (9.4)	1.49 (1.16-1.91)	.002
Early acute noninfectious conditions	77 (35.8)	98 (46.0)	1.69 (1.06–2.68)	.02
Initial combination antibiotic therapy	210 (97.7)	181 (85.0)	0.164 (0.05-0.51)	.002
Indwelling catheter	68 (31.6)	39 (18.3)	0.50 (0.30-0.85)	.01

Goodness of fit (Hosmer-Lemeshow) chi-square p value = .64. Area under the receiver operating characteristic curve = .74.

- Antibiothérapie dans l'heure
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- Isolement protecteur?

Bénéfice et risques de l'isolement

Il y a plus de 40 ans...



Il y a plus de 40 ans...

- La plupart des études positives sont anciennes
- La quasi-totalité des études sont réalisée chez les patients à très haut risque infectieux (R4)
- Elles évaluent un isolement complet :
 - Isolement géographique
 - Filtre à haute efficience
 - Décontamination digestive
 - +/- une antibioprophylaxie

Il y a plus de 40 ans...

- Les études évaluant un isolement simplifié sont négatives
- Isolement sans DDS
- Isolement sans HEPAF
- Isolement dans des groupes de plus faible risque infectieux (LNH)
- Absence de bénéfice sur la mortalité ou le risque infectieux d'un isolement simplifié
- Seule exception:
- Possible efficacité de la filtration à haute efficience
- Au cours de l'allogreffe de moelle
- Avant l'avènement de la prophylaxie antifongique

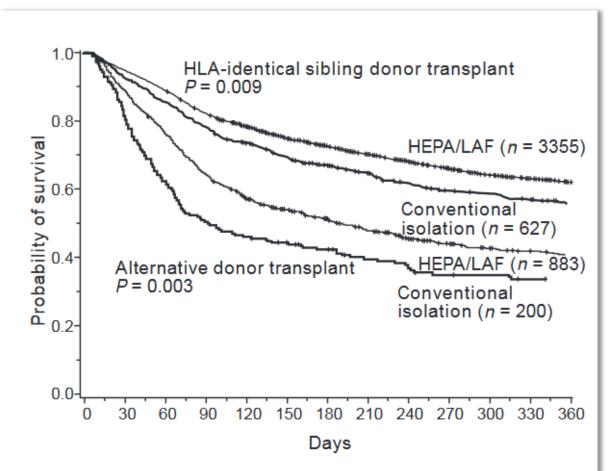
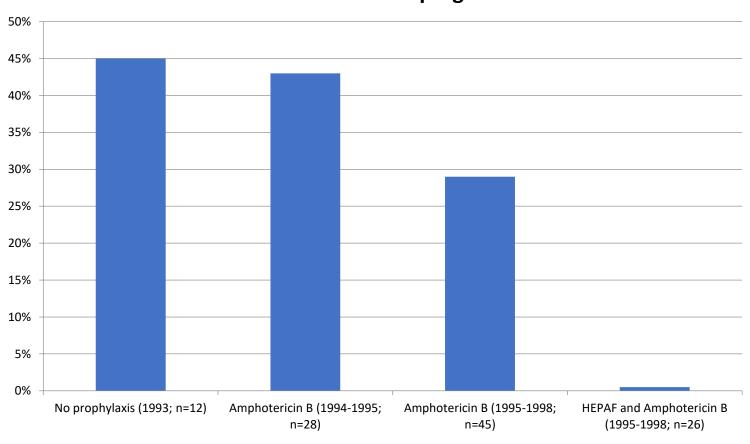
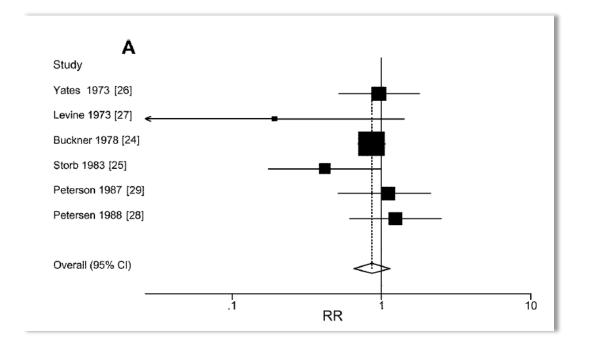


Figure 1 Probability of survival in the first year post-transplant after HLA-identical sibling transplant and alternative donor transplant by type of protective isolation.

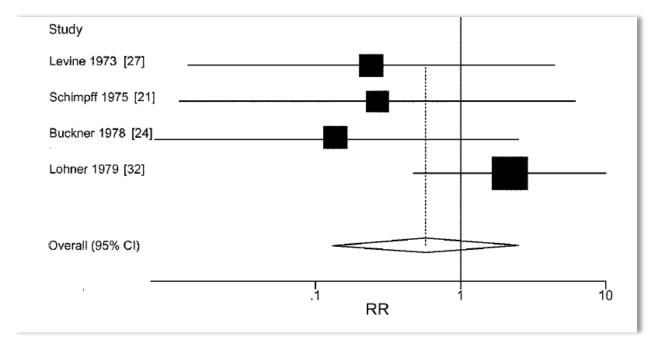
Rate of invasive aspergillosis



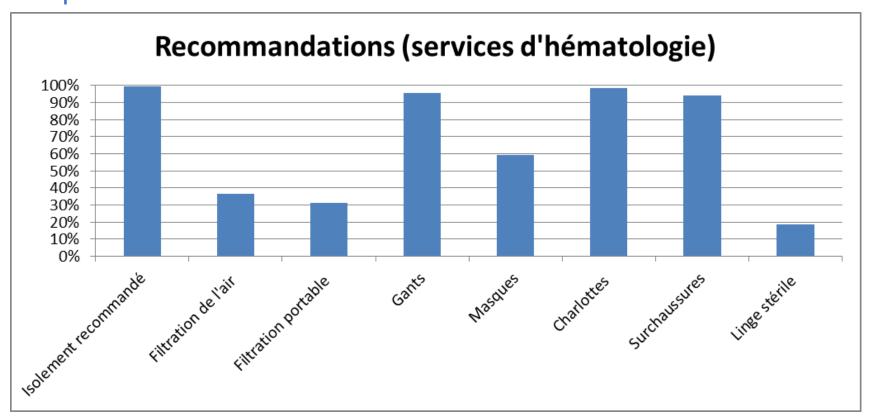
Isolement et mortalité



Isolement et infection fongique



Enquête nationale SF2H





II. Prophylaxis and protective isolation

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

RII-2—Protective isolation should not be considered as a sterile isolation (Grade 1-, strong agreement)

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

Bas niveau de preuve, rapport bénéfice risque incertain: études nécessaires

Quand on est isolé on est moins surveillé

	Genera	l Cohort		ive Heart Cohort	Isolated Patients vs		
Measures	Isolated Patients (n = 78)	Control Patients (n = 156)	Isolated Patients (n = 72)	Control Patients (n = 144)	Control Patients Test Statistic (95% CI)†	ts* P Value	
No. of daily vital signs expected	3.2	3.1	4.7	4.2	0.32 (0.11 to 0.53)	.003	
No. of daily vital signs recorded	2.6	3.0	6.2	6.3	-0.21 (-0.54 to 0.12)	.21	
Vital signs incompletely recorded, %	10	8	19	10	1.92 (1.61 to 2.30)	<.001	
Days with no vital signs recorded, %	6	f	5	1	2.55 (1.14 to 5.69)	.02	
Vital signs with respiratory rate of 20/min, %	41	39	43	36	1.07 (0.93 to 1.23)	.34	
Days with vital signs not recorded as ordered, %	58	41	43	21	2.76 (2.17 to 3.51)	<.001	
Days with no nursing narrative notes, %	11	11	17	9	1.77 (1.40 to 2.24)	<.001	
Days with no physician progress notes, %	43	24	7	2	2.91 (1.90 to 4.47)	<.001	

	General	Cohort	Congestive Heart Failure Cohort		Isolated Patients vs	
Measures	Isolated Patients (n = 78)	Control Patients (n = 156)	Isolated Patients (n = 72)	Control Patients (n = 144)	Rate Ratio (95% CI)	P Value
Length of stay, median (IQR), d	31 (10-69)	12 (7-24)	B (4-13)	6 (4-9)	NA	<.0011
Adverse events, No. (rate per 1000 d) Any	70 (17.0)	25 (7.0)	38 (47.3)	28 (24.5)	2.20 (1.47-3.30)	<.001
Nonpreventable	19 (4.6)	16 (4.5)	15 (18.7)	23 (20.1)	0.99 (0.54-1.81)	.98
Preventable	51 (12.4)	9 (2.5)	23 (28.6)	5 (4.4)	6.96 (3.38-14.3)	<.001

Conclusion

Conclusions

• Isolement recommandé, sans retarder l'admission ou nuire à la

surveillance, pour les patients

1/ Ayant une neutropénie profonde (<500/mm3)

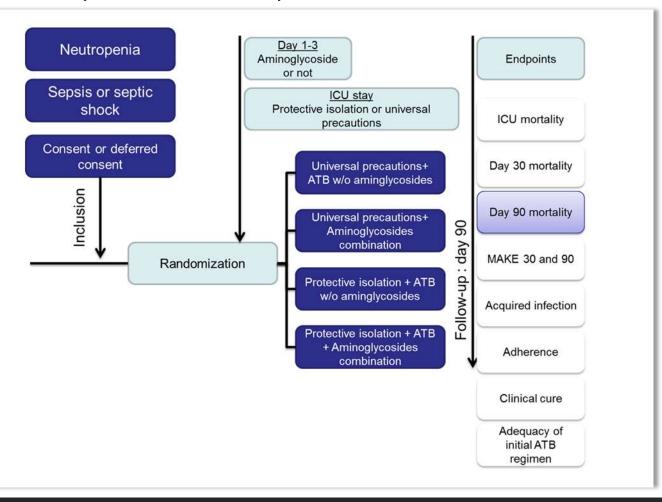
2/ Prolongée (>7j de neutropénie attendue)

3/ Isolement comportant autant que possible :

- 1. High-efficiency air filtration [filtration of 99.7 % of particles greater than or equal to 0.3 μ m; International Organization for Standardization (ISO) class 5 or better]
- 2. Geographic isolation
- 3. Technical isolation, including a face mask and a cap

Etude combination-Lock

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Merci de votre attention

