Nouveautés en 2015

« Immunodéprimés »

Dr Rivière Frédéric
Service Pneumologie
Hôpital Percy
Clamart

Introduction

- Vaste champs d'investigation hétérogène
- Milliers de publications d'intérêt variable

- Plan (Segmentation par groupe de pathogènes)
  - Epidémiologie
    - Champignons - PCP - Mycobactérie
  - Imagerie (apport du TEP?)
  - Diagnostic microbiologique
    - Bactérie - Champignons - PCP
  - Traitement
    - Curatif (antifongique)
    - Prophylactique (antifongique)
  - Voyage

Epidémiologie

Infection Fongique Invasive Non Aspergillaire

Bone Marrow Transplantation (2015), 1–6

www.nature.com/bmt

ORIGINAL ARTICLE

Risk factors and impact of non-*Aspergillus* mold infections following allogeneic HCT: a CIBMTR infection and immune reconstitution analysis

ML Riches[1], S Trifilio[2], M Chen[3], KW Ahn[3,4], A Langston[5], HM Lazarus[6], DI Marks[7], R Martino[8], RT Maziarz[9], GA Papincolou[10], JR Wingard[11], J-AH Young[12] and CL Bennett[13]

- Etude rétrospective, multicentrique
- 1iere année ACSH
  - Fusariose: 52 (28 j post ACSH)
  - Mucormycose: 72 (75j post ACSH)
  - Contrôle: 11856

Table 1. Pre-transplant characteristics of patients with mucormycosis, fusariosis and controls

Variable N *(%)*	*Mucormycosis* (n = *72*)	*Fusariosis* (n = *52*)	*Controls* (n = *11 856*)	P-*value*
Age, years (median (range))	47 (3–68)	32 (1–63)	34 (< 1–79)	< 0.001
KPS at HCT				0.048
⩾ 90%	40 (56%)	31 (60%)	8049 (68%)	
< 90%	30 (42%)	20 (38%)	3330 (28%)	
Unknown	2 (3%)	1 (2%)	477 (4%)	

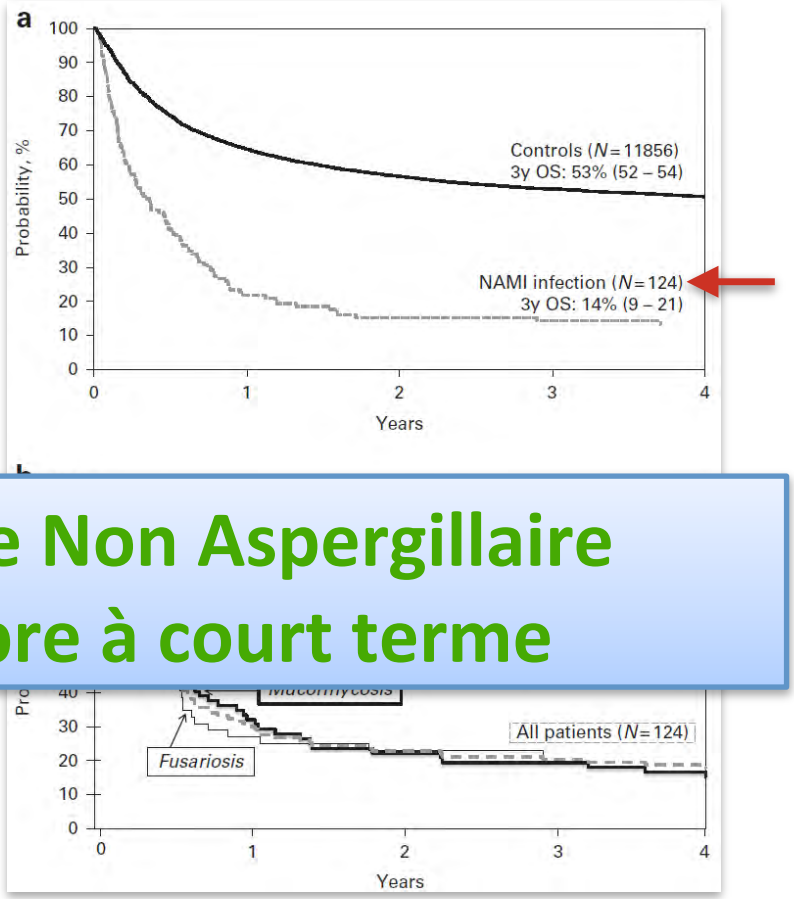
Table 2. Frequency of systemic antifungal prophylaxis administered

Antifungal prophylaxis N *(%)*	*Mucormycosis* (n = *72*)	*Fusariosis* (n = *52*)	*Controls* (n = *11 856*)	P-*value*
				0.549
Azoles				0.148
Fluconazole	29 (40%)	28 (54%)	6264 (53%)	
Voriconazole	8 (11%)	1 (2%)	683 (6%)	
Itraconazole	5 (7%)	2 (4%)	512 (4%)	
Posaconazole	1 (1%)	0	74 (< 1%)	
Amphotericin	14 (19%)	13 (25%)	1782 (15%)	
Echinocandin	1 (1%)	0	158 (1%)	
Other agent (including clinical trial)	1 (1%)	2 (4%)	319 (3%)	
None	13 (18%)	6 (12%)	2000 (17%)	

Infection Fongique Invasive Non Aspergillaire

Table 3. Multivariable analysis for risk factors for development of mucormycosis in the first year after transplant

Variable	*RR for mucormycosis (95% CI)*	*P-value*
Acute GvHD grade II–IV		0.027
No	1.00	
Yes	1.78 (1.07–2.98)	
Prior *Aspergillus* infection		0.0007
No	1.00	
Yes	4.91 (1.96–12.28)	
Age (years)		0.0006
⩽50	1.00	



Infection Fongique Invasive Non Aspergillaire
Rare mais Pronostic sombre à court terme

Table 5. Primary COD reported for deceased patients in this analysis

Primary COD	*Mucormycosis (n = 62)*	*Fusariosis (n = 46)*	*Controls (n = 5947)*
Infection	32 (52%)	23 (50%)	1141 (19%)
Relapse	10 (16%)	5 (11%)	2227 (37%)
GvHD	6 (10%)	5 (11%)	690 (12%)
Organ failure	11 (18%)	6 (13%)	877 (15%)
Other	3 (5%)	7 (15%)	898 (15%)

Abbreviation: COD = cause of death.

PCP et connectivites

Contents lists available at ScienceDirect
Seminars in Arthritis and Rheumatism
journal homepage: www.elsevier.com/locate/semarthrit

Pneumocystis jirovecci pneumonia in connective tissue diseases: Comparison with other immunocompromised patients

Andrew J. Teichtahl, (MBBS, BPhysio, FRACP, PhD)[a,b,*], Kathleen Morrisroe, (MBBS)[a,1], Sabina Ciciriello, (MBBS, FRACP, PhD)[a], Ian Jennens, (MBBS, FRACP)[c], Susan Tadros, (MBBS, BSc, MRCP)[a], Ian Wicks, (MBBS, FRACP, PhD)[a,d,e,*]

- Etude rétrospective monocentrique
- IF+ et/ou PCR++
- 90 patients
  - 39 (43%) VIH
  - 16 (18%) hémopathies
  - 14 (16%) cancers
  - 7 (8%) transplantés rénaux
  - 3 (3%) MICI
  - 11 (12%) connectivites (dont 1 pentamidine, pas de données d'observance)

dont 2 Cotrimoxazole (observance?)

Risque de PCP et connectivites: Prophylaxie+++

	Total cohort (N = 90)	CTD (n = 11)	Non-CTD (n = 79)	p
Lymphocytes ($\times 10^9$/L)	0.53 (0.56)	0.18 (0.16)	0.57 (0.57)	< 0.001
Haemoglobin (g/L)	108.5 (20.3)	109.7 (26.0)	108.4 (19.6)	0.871
Leucocytes ($\times 10^9$/L)	7.9 (4.6)	7.1 (3.6)	8.0 (4.8)	0.455
Platelets ($\times 10^9$/L)	240 (133)	236 (130)	241 (135)	0.917
Neutrophils ($\times 10^9$/L)	6.5 (4.2)	5.8 (3.5)	6.6 (4.2)	0.488
eGFR	74 (23)	61 (20)	76 (22)	0.039
ESR (n = 24) (mm/h)	83.7 (45.0)	95.7 (50.1)	78.1 (42.7)	0.406
CRP (n = 71) (mg/L)	109.5 (95.7)	174 (124)	98 (86)	0.076
ALP (n = 80) (IU/L)	141.9 (159.1)	98 (71)	148 (167)	0.107
AST (n = 76) (IU/L)	44.6 (27.6)	47 (33)	44 (27)	0.796
ALT (n = 80) (IU/L)	38.9 (44.7)	34 (23)	37 (24)	0.562
Albumin (n = 80) (g/L)	26.1 (5.9)	27 (7)	26 (6)	0.858
PJP prophylaxis (%)[a]	2 (3.0)[d]	1 (9.1)	1 (1.8)[c]	0.20
Corticosteroid exposure[a]	31 (45.6)[c c]	11 (100)	20 (35.1)[c]	< 0.001
Corticosteroid dose (mg)[b]	8.9 (20.1)[d]	15.5 (12.3)	7.6 (21.2)[c]	0.11
Iatrogenic exposure to other immunosuppressants[a]	24 (26.7)[d]	10 (90.9)	14 (24.6)[c]	< 0.001
Mortality, n (%)[a]	5 (5.6)	3 (27.3)	2 (2.5)	0.001

PCP et Transplantation d'organe

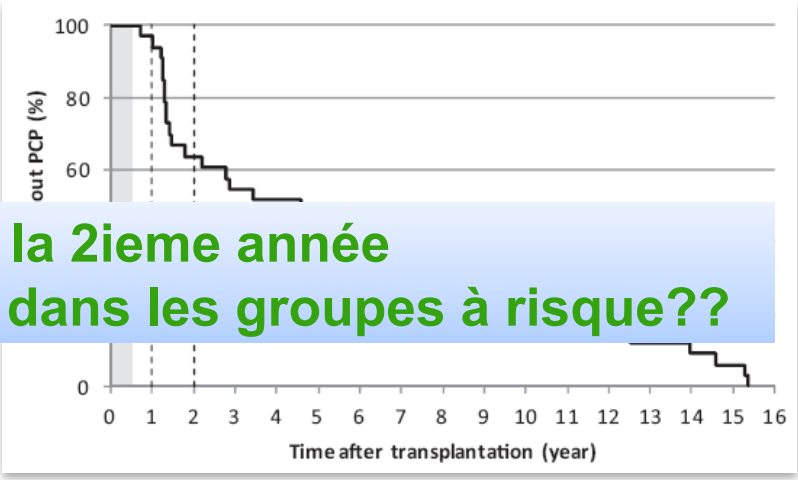
American Journal of Transplantation 2015; 15: 190–199
Wiley Periodicals Inc.

doi: 10.1111/ajt.12947

Risk Factors of *Pneumocystis* Pneumonia in Solid Organ Recipients in the Era of the Common Use of Posttransplantation Prophylaxis

- Etude rétrospective, monocentrique - Cas Témoins (1/2)
- 99 transplantés d'organe:70% rein, 15% cœur, 15% foie (33 PCP)

- Prophylaxie par Cotrimoxazole
  - 6 premiers mois post transplantation



SurRisque PCP lors de la 2ieme année
Discussion prophylaxie, notamment dans les groupes à risque??

- Analyse multivariée
  - Age>65 ans (OR: 3.7)
  - Infection CMV (OR: 5.2)
  - Lymphocytes totaux <750 (OR: 3.9)

	SOT recipients who would have benefited from a PCP prophylaxis in the period of 180 days before D0		
Criteria of establishment of prophylaxis	With PCP, n = 33	Without PCP, n = 66	p-Value
Patient ≥65 years old in the second year after transplantation, n (%)	8 (24.2%)	9 (13.6%)	0.187[1]
Patient with lymphocytes <750/mm^3 for more than 1 month, n (%)	10 (30.3%)	11 (16.7%)	0.118[1]
Patient with detectable CMV viremia, n (%)	16 (48.5%)	8 (12.1%)	**<0.001**[1]
All these criteria, n (%)	23 (70.0%)	20 (30.3%)	**<0.001**[1]

PCP: maladie contagieuse?

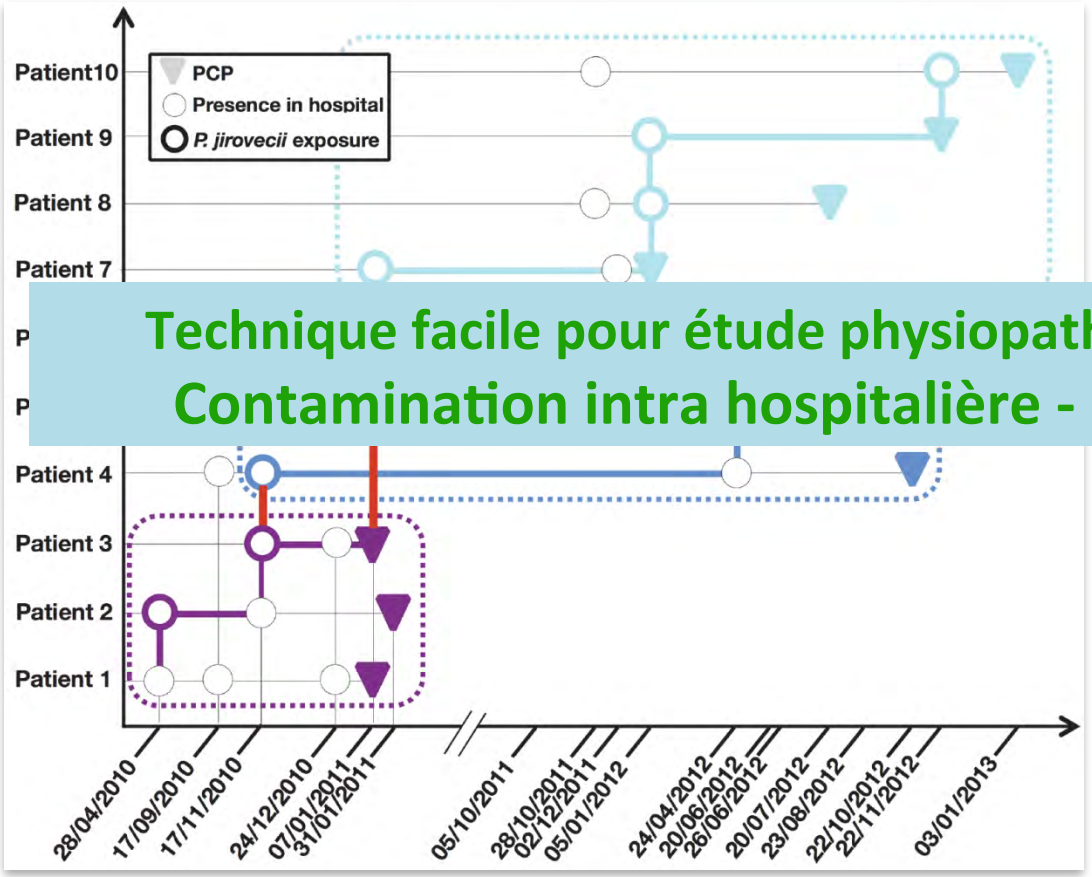
- 91 patients
  - (45%VIH, 27% Hémopathies, 16% Transplantés rénaux, 12% autres)
- Identification de Short-Tandem-Repeat loci

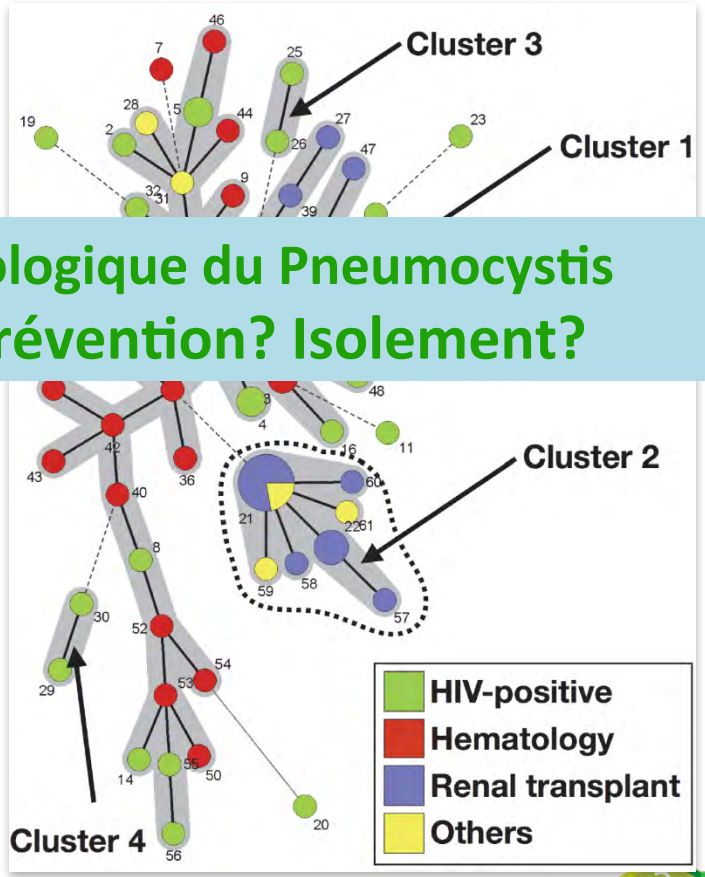
PLOS ONE

RESEARCH ARTICLE

New Short Tandem Repeat-Based Molecular Typing Method for *Pneumocystis jirovecii* Reveals Intrahospital Transmission between Patients from Different Wards

Maud Gits-Muselli[1], Marie-Noelle Peraldi[2,3], Nathalie de Castro[4], Véronique Delcey[5], Jean Menotti[1,3,6,7], Nicolas Guigue[1,3], Samia Hamane[1], Emmanuel Raffoux[8], Anne Bergeron[3,9], Sandrine Valade[10], Jean-Michel Molina[3,4], Stéphane Bretagne[1,3,6,7], Alexandre Alanio[1,3,6,7]*





Technique facile pour étude physiopathologique du Pneumocystis

Contamination intra hospitalière - Prévention? Isolement?

- Délai médian entre exposition et PCP: 197 jours

Tableau atypique de la Tuberculose de l'ID

ORIGINAL ARTICLE INFECTIOUS DISEASES

Clinical features and outcomes of tuberculosis in transplant recipients as compared with the general population: a retrospective matched cohort study

Clin Microbiol Infect. 2015; 21(7): 651-8

- Etude rétrospective, cas témoin (1/4)
- 22 transplantés d'organe avec diagnostic de tuberculose

Characteristics	Transplant recipients (n = 22), no. (%)	Patients from the general population (n = 88), no. (%)	RR (95% CI)	p
Clinical manifestations				
Fever	17 (81)	42 (49.4)	8.5 (1.81–39.81)	0.002
Constitutional symptoms[a]	9 (45)	54 (63.5)	0.57 (0.22–1.48)	0.207
Cough	9 (45)	53 (62.4)	0.6 (0.21–1.49)	0.245
Dyspnoea	1 (5)	13 (15.3)	0.27 (0.03–2.41)	0.396
Pleuritic chest pain	1 (5)	15 (17.6)	0.4 (0.05–3.04)	0.287
Haemoptysis	1 (5)	23 (27.1)	0.11 (0.01–1.11)	0.070
Symptoms suggestive of epididymo-orchitis	3 (15)[b]	0 (0)	—	0.004
Monoarticular or oligoarticular pain	2 (10)	1 (1.2)	8 (1.01–88.22)	0.043
Dysphonia	1 (5)	4 (4.7)	1 (0.08–12.56)	1.000
Other clinical manifestations	5 (25)[c]	4 (4.7)[d]	9 (1.57–51.74)	0.004
Physical findings	13 (65)	27 (31.4)	5.33 (1.55–18.39)	0.007
Ascites	7 (35)[e]	0 (0)	—	<0.001
Findings consistent with epididymo-orchitis	3 (15)[b]	0 (0)	—	0.004
Monoarthritis or oligoarthritis	2 (10)	1 (1.2)	8 (1.01–88.22)	0.043
Rales on chest examination	1 (5)	14 (16.3)	0.29 (0.04–2.04)	0.346
Findings consistent with pleural effusion	1 (5)	3 (3.5)	2 (0.18–22.06)	0.564
Peripheral lymphadenopathy	1 (5)	8 (9.3)	0.43 (0.04–4.29)	0.861
Tuberculosis form				
Pulmonary	12 (54.5)	77 (87.5)	0.12 (0.03–0.44)	0.001
Extrapulmonary	5[f] (22.7)	7[g] (8)	3.17 (0.94–10.70)	0.055
Disseminated	5[h] (22.7)	4[i] (4.5)	6.33 (1.29–31.11)	0.005
Number of involved organs				
Two or more organs involved with a definitive diagnosis	4 (18.2)	3 (3.4)	6.30 (1.30–30.60)	0.045
Two or more organs involved with a probable diagnosis	8 (36.4)	10 (11.4)	5.40 (1.64–17.77)	0.003
Chest radiograph findings				
None	6 (28.6)	5 (5.7)	5.75 (1.57–21.02)	0.003
Unilateral vs. bilateral pulmonary infiltrates[j]	10 (66.7)	44 (56.4)	1.55 (0.48–4.95)	0.653
Cavitary infiltrates[j]	0 (0)	50 (64.1)	—	<0.001
Diffuse infiltrates vs. focal infiltrates[j]	5 (33.3)	0 (0)	—	<0.001
Pleural effusion	1 (5)	3 (3.5)	2 (0.181–22.156)	0.571

Tableau atypique de la Tuberculose de l'ID

Variable	Transplant recipients (n = 22)	Patients from the general population (n = 88)	RR (95% CI)	p
Diagnosis of tuberculosis				
Median time (days) from onset of symptoms to diagnosis (IQR)	70 (48)	46 (70)	—	0.076
Median time (days) from clinical suspicion of tuberculosis to definitive diagnosis (IQR)	14 (51.5)	0 (1.25)	—	0.001
Sputum culture performed, no. (%)	12 (54.5)	77 (87.5)	0.17 (0.06–0.49)	<0.001
Positive sputum culture, no. (%)	10 (83.3)	70 (90.9)	0.5 (0.09–2.75)	0.769
Invasive procedures required, no. (%)	12 (54.5)[a]	15 (17)[b]	5.84 (2.14–15.98)	0.001
Post-mortem diagnosis, no. (%)	3 (13.6)[c]	0 (0)	—	<0.001

Risk factor	Adjusted hazard ratio (95% CI)	p
Transplantation	1.11 (0.06–21.43)	0.943
Age (years)	1.58 (0.38–6.51)	0.529
Charlson comorbidity score ≥2	8.03 (0.32–203.41)	0.206
Number of organs with tuberculosis involvement	10.14 (1.06–97.16)	0.045

- Toxicité médicamenteuse (p: 0.014)
  - 10% non transplanté vs 38% transplanté

- Aucune différence de la Mortalité après diagnostic de tuberculose (p: 0.057)

Tuberculose et ID: Y Penser

Imagerie

Place de la TEP et Infections pulmonaires (ID)?

F-FDG-PET/CT imaging in patients with febrile neutropenia and hematological malignancies.

Camus et Al. Anticancer Res. 2015; 35(5): 2999-3005

- Etude prospective, monocentrique
- 48 patients consécutifs, hémopathies malignes et neutropénie fébrile persistante

Apport du TEP peu évident
Problème de disponibilité en urgence
Pas de diagnostic microbiologique

Pas de distinction du TEP selon le pathogène

  - 3% KTC
  - 3% vésiculaires
- 38 patients cliniquement symptomatiques
  - 23 TEP
  - Sensibilité: 61%

Diagnostic

LBA et diagnostic bactériologique

Mediterranean Journal of Hematology and Infectious Diseases

Original Article

Diagnostic Value of Bronchoalveolar Lavage in Leukemic and Bone Marrow Transplant Patients: The Impact of Antimicrobial Therapy

Abraham Tareq Yacoub[1], Dani Thomas[2], Carol Yuan[2], Carolina Collazo[3], John Greene[2], Frank Walsh[2], David Solomon[2], Skai Schwartz[2] and Arthur Andrews[4]

- Etude rétrospective monocentrique
- 297 patients
  - 42% ACSH
  - 58% hémopathies malignes
  - VIH-
  - LBA (2x60cc)
  - 107 LBA+ (36%)

Time on antibiotics (hrs)	Positive BAL/number patients (%)	p value
None	3 / 4 (75.0)	
24-48 hours	16/ 52 (30.8)	NS
>48 hours w/o change	27/ 89 (30.3)	
>48h, but with change	42/118 (35.6)	
0-24 hours	21/37 (56.8)	<0.01
> 24 hours	85/259 (32.8)	

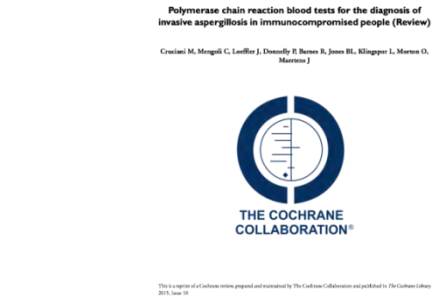
Intérêt de LBA si réalisé précocément (<24h d'ATB)

Aspergillose Pulmonaire Invasive – dépistage AGAS et/ou PCR?

Galactomannan and Polymerase Chain Reaction-Based Screening for Invasive Aspergillosis Among High-Risk Hematology Patients: A Diagnostic Meta-analysis.
Arvanitis et al. Clinical Infectious Diseases. 61(8):1263-1272,

Table 2. Results of Basic Analysis

Test	Sensitivity, % (95% CI)	Specificity, % (95% CI)	Positive LR (95% CI)	Negative LR (95% CI)
PCR	84 (71–92)	76 (64–85)	3.5 (2.3–5.4)	0.21 (.11–.39)
2 PCRs	57 (40–72)	93 (87–97)	8.4 (4.2–17.1)	0.46 (.32–.67)
GM	92 (83–96)	90 (81–95)	9.3 (4.6–18.7)	0.09 (.04–.18)
2 GMs	62 (48–74)	95 (91–97)	12.1 (6.3–23.3)	0.40 (.29–.57)
GM or PCR	99 (96–100)	64 (49–77)	2.8 (1.9–4.1)	0.02 (.01–.06)
GM and PCR	68 (54–80)	98 (94–100)	43.2 (12.6–148)	0.32 (.21–.49)

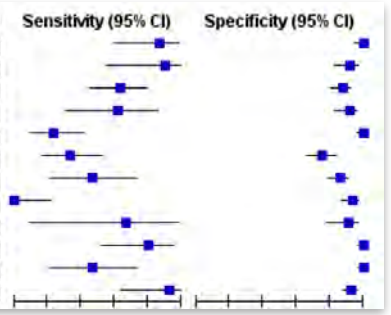

Polymerase chain reaction blood tests for the diagnosis of invasive aspergillosis in immunocompromised people (Review)

Cruciani M, Mengoli C, Loeffler J, Donnelly P, Barnes R, Jones BL, Klingspor L, Morton O, Maertens J

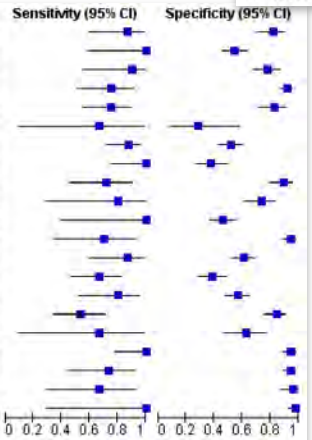
THE COCHRANE COLLABORATION®

This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in The Cochrane Library 2015, Issue 10

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Badie 2010	13	0	2	67	0.87 [0.60, 0.98]	1.00 [0.95, 1.00]
Cuenca-Estrella 2009	9	6	1	67	0.90 [0.55, 1.00]	0.92 [0.83, 0.97]
Florent 2006	21	17	12	117	0.64 [0.45, 0.80]	0.87 [0.80, 0.92]
Halliday 2006	8	7	5	75	0.62 [0.32, 0.86]	0.91 [0.83, 0.96]
Rogers 2013	7	0	23	102	0.23 [0.10, 0.42]	1.00 [0.96, 1.00]
Rogers 2013	10	25	20	77	0.33 [0.17, 0.53]	0.75 [0.66, 0.83]
Rogers 2013	7	18	8	113	0.47 [0.21, 0.73]	0.86 [0.79, 0.92]
Rogers 2013	0	9	15	122	0.00 [0.00, 0.22]	0.93 [0.87, 0.97]
Springer 2011	2	4	1	39	0.67 [0.09, 0.99]	0.91 [0.78, 0.97]
Suarez 2008	12	0	3	109	0.80 [0.52, 0.96]	1.00 [0.97, 1.00]
Suarez 2008	7	0	8	109	0.47 [0.21, 0.73]	1.00 [0.97, 1.00]
White 2006	12	14	1	175	0.92 [0.64, 1.00]	0.93 [0.88, 0.96]



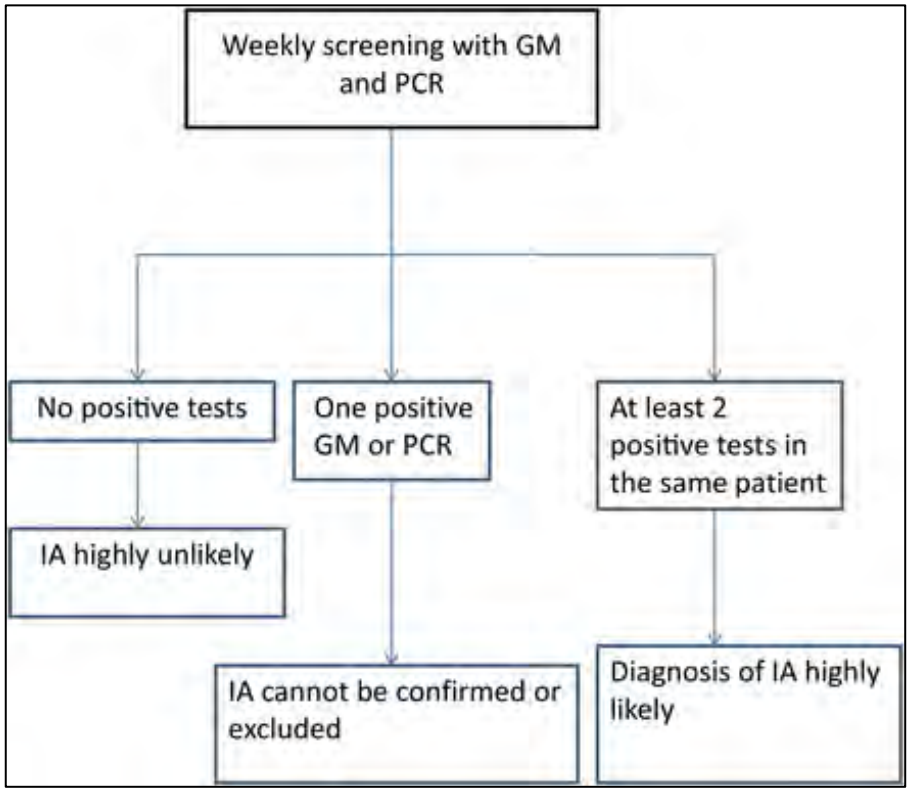
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Badie 2010	13	12	2	55	0.87 [0.60, 0.98]	0.82 [0.71, 0.90]
Barnes 2009	7	53	0	64	1.00 [0.59, 1.00]	0.55 [0.45, 0.64]
Cuenca-Estrella 2009	9	16	1	57	0.90 [0.55, 1.00]	0.78 [0.67, 0.87]
da Silva 2010	15	14	5	159	0.75 [0.51, 0.91]	0.92 [0.87, 0.96]
El Mahallawy 2006	21	11	7	52	0.75 [0.55, 0.89]	0.83 [0.71, 0.91]
Ferns 2002	2	10	1	4	0.67 [0.09, 0.99]	0.29 [0.08, 0.58]
Florent 2006	29	65	4	69	0.88 [0.72, 0.97]	0.51 [0.43, 0.60]
Halliday 2006	13	51	0	31	1.00 [0.75, 1.00]	0.38 [0.27, 0.49]
Hebart 2000a	13	8	5	66	0.72 [0.47, 0.90]	0.89 [0.80, 0.95]
Hummel 2009	4	17	1	48	0.80 [0.28, 0.99]	0.74 [0.61, 0.84]
Landlinger 2010	4	65	0	56	1.00 [0.40, 1.00]	0.46 [0.37, 0.56]
Ramírez 2009	7	6	3	109	0.70 [0.35, 0.93]	0.95 [0.89, 0.98]
Rogers 2013	13	51	2	80	0.87 [0.60, 0.98]	0.61 [0.52, 0.69]
Rogers 2013	20	63	10	39	0.67 [0.47, 0.83]	0.38 [0.29, 0.48]
Rogers 2013	12	57	3	74	0.80 [0.52, 0.96]	0.56 [0.48, 0.65]
Rogers 2013	16	16	14	86	0.53 [0.34, 0.72]	0.84 [0.76, 0.91]
Springer 2011	2	16	1	27	0.67 [0.09, 0.99]	0.63 [0.47, 0.77]
Suarez 2008	15	6	0	103	1.00 [0.78, 1.00]	0.94 [0.88, 0.98]
Suarez 2008	11	6	4	103	0.73 [0.45, 0.92]	0.94 [0.88, 0.98]
Sugawara 2013	6	2	3	53	0.67 [0.30, 0.93]	0.96 [0.87, 1.00]
von Lilienfeld-Toal 2009	3	3	0	113	1.00 [0.29, 1.00]	0.97 [0.93, 0.99]



GREPI
Groupe pour la Recherche et l'Enseignement en Pneumo-Infectiologie

3es JOURNÉES du GREPI

Aspergillose Pulmonaire Invasive - Reproductibilité AGAS



Hétérogènéité
Standardisation des PCR!!!

Aspergillose Pulmonaire Invasive – Reproductibilité AGAS

PLOS ONE

RESEARCH ARTICLE

Importance of Operational Factors in the Reproducibility of *Aspergillus* Galactomannan Enzyme Immune Assay

Nicolas Guigue[1,2], Samuel Lardeux[3], Alexandre Alanio[1,2,4,5], Samia Hamane[1], Marc Tabouret[3], Stéphane Bretagne[1,2,4,5]*

- AGAS – Coefficient de variation~14,5%
- 550 sera

Day 0

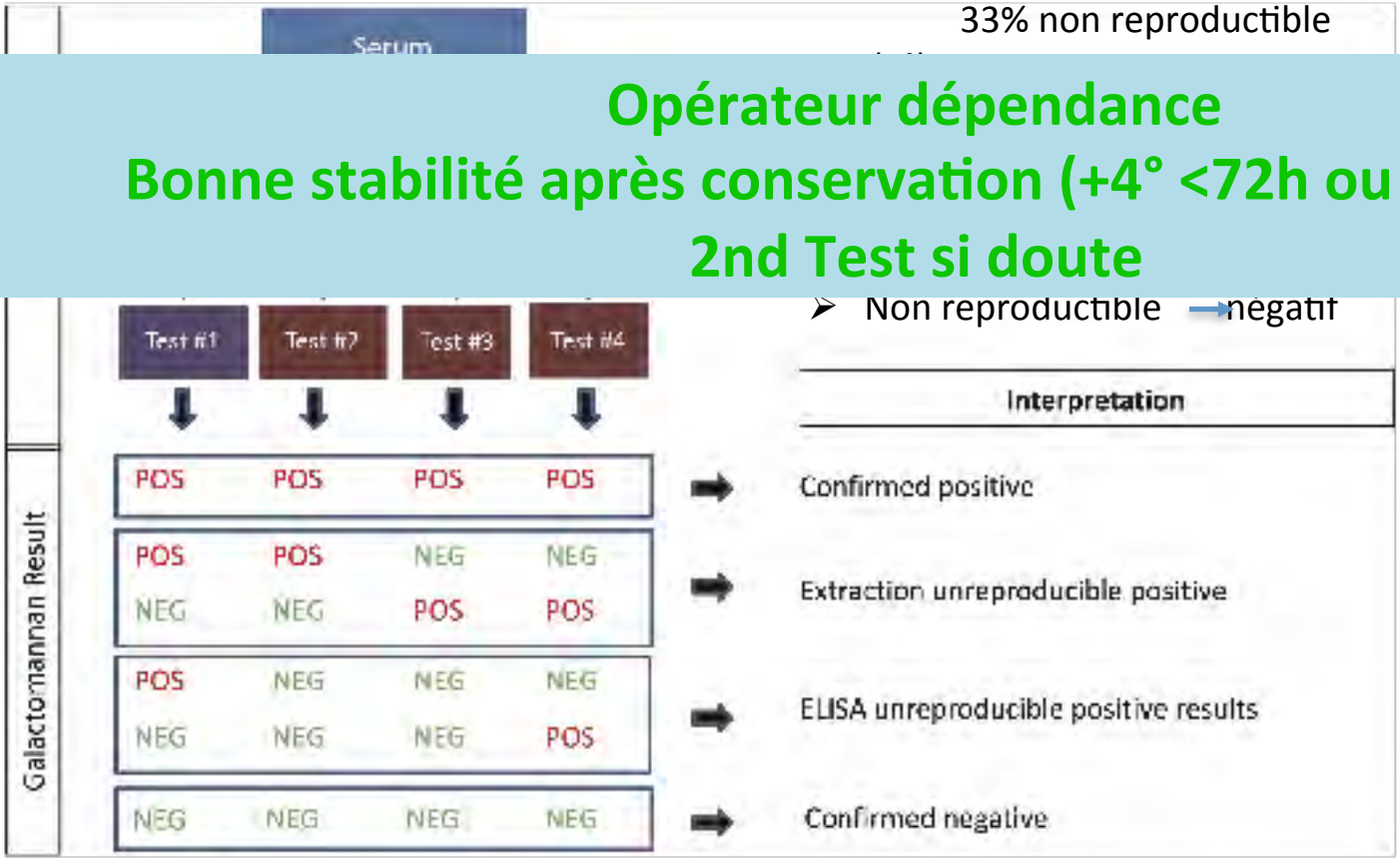
- 94,5% -
- 5,5% au moins 1+
  - 50% +
  - 17% non conclusive
  - 33% non reproductible

Opérateur dépendance

Bonne stabilité après conservation (+4° <72h ou -20° 8mois)

2nd Test si doute

- Non reproductible → négatif



GREPI

3es JOURNÉES du GREPI

Infection fongique Invasive et Intérêt de la PCR - Dépistage

Springer J et al. Clin Microbiol Infect. 2015 Sep 21.

- Etude prospective, multicentrique
- PCR « maison »
- Population
  - ACSH et Leucémie aigue
- 2128 serum – 213 patients

PCR en dépistage IFI (sans prophylaxie)
Pb de Standardisation

Biomarker performance in patients with probable IA

Evaluation of biomarkers	Centre without primary antifungal prophylaxis (UKW)					Centres with primary antifungal prophylaxis (MUI and HEL)				
	1 × GM+[b]	1 × PCR+[c]	2 × PCR+[d]	GM/1 × PCR	GM/2 × PCR	1 × GM+[e,f]	1 × PCR+[c]	2 × PCR+[d]	GM/1 × PCR[g]	GM/2 × PCR[h]
True positives (*n*)	14	13	10	13	10	4	4	2	4	2
True negatives (*n*)	73	57	72	75	76	53	20	38	55	60
False positives (*n*)	5	21	6	3	2	20	53	35	18	13
False negatives (*n*)	0	1	4	1	4	0	0	2	0	2
Sensitivity, % (95% CI)	100.0 (76.8–100.0)	92.9 (66.1–99.8)	71.4 (41.9–91.6)	92.9 (66.1–99.8)	71.4 (41.9–91.6)	100.0 (39.8–100.0)	100.0 (39.8–100.0)	50.0 (6.8–93.2)	100.0 (39.8–100.0)	50.0 (6.8–93.2)
Specificity, % (95% CI)	93.6 (85.7–97.9)	73.1 (61.8–82.5)	92.3 (84.0–97.1)	96.2 (89.2–99.2)	97.4 (91.0–99.7)	72.6 (60.9–82.4)	27.4 (17.6–39.1)	52.1 (40.0–63.9)	75.3 (63.9–84.7)	82.2 (71.5–90.2)
PPV, % (95% CI)	73.7 (48.8–90.9)	38.2 (22.2–56.4)	62.5 (35.4–84.8)	81.3 (54.4–96.0)	83.3 (51.6–97.9)	16.7 (4.7–37.4)	7.0 (1.9–17.0)	5.4 (0.7–18.2)	18.2 (5.2–40.3)	13.3 (1.7–40.5)
NPV, % (95% CI)	100.0 (95.1–100.0)	98.3 (90.8–100.0)	94.7 (87.1–98.5)	98.7 (92.9–100.0)	95.0 (87.7–98.6)	100.0 (93.3–100.0)	100.0 (83.2–100.0)	95.0 (83.1–99.4)	100.0 (93.5–100.0)	96.8 (88.8–99.6)

Infection fongique Invasive et Intérêt de la PCR - Identification

Alanio A et al. Clin Microbiol Infect. 20115; 21(6): 594.

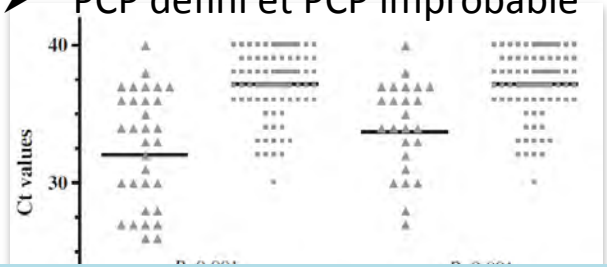
- Etude monocentrique, rétrospective
- 19 biopsies (13 patients): Mucorale
- PCR Electrospray-ionization mass spectrometry vs Culture/qPCR tps réel/PCR 18S/PCR ITS

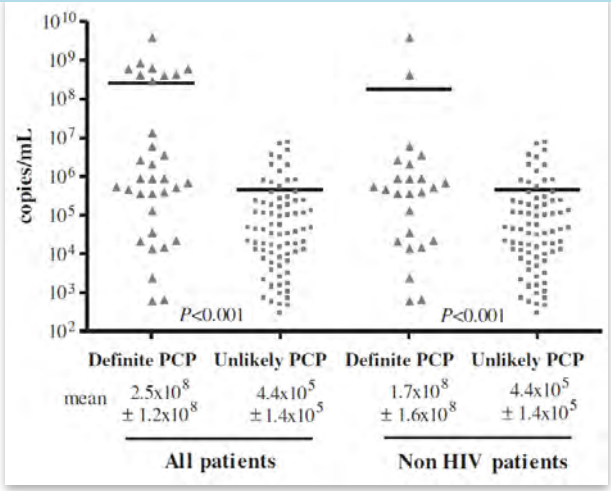
	PCR-ESI MS	qPCR	ITS PCR	18S PCR
Kappa statistics				
Genus-level identification	0.80	0.76	0.49	0.37
Species level identification	0.72	/[a]	0.14	no identification[b]

PCR- Rôle fondamental pour **l'identification**
mais Coût important (PlexID°)

PCP et place de la PCR?

- Etude prospective, monocentrique
- 120 patients
- Evaluation PCR « maison » et PCR commerciale
- Diagnostic clinico-radio-évolutif sous TTT
  - PCP défini et PCP improbable





Diagnostic Microbiology and Infectious Disease 82 (2015) 143–147

Contents lists available at ScienceDirect

Diagnostic Microbiology and Infectious Disease

journal homepage: www.elsevier.com/locate/diagmicrobio

Comparison of 2 real-time PCR assays for diagnosis of *Pneumocystis jirovecii* pneumonia in human immunodeficiency virus (HIV) and non-HIV immunocompromised patients

Isabel Montesinos [a,*], Françoise Brancart [a], Kinda Schepers [b], Frederique Jacobs [b], Olivier Denis [a], Marie-Luce Delforge [a]

Clinical and demographic characteristics of patients and results of different techniques used for PCP diagnosis.

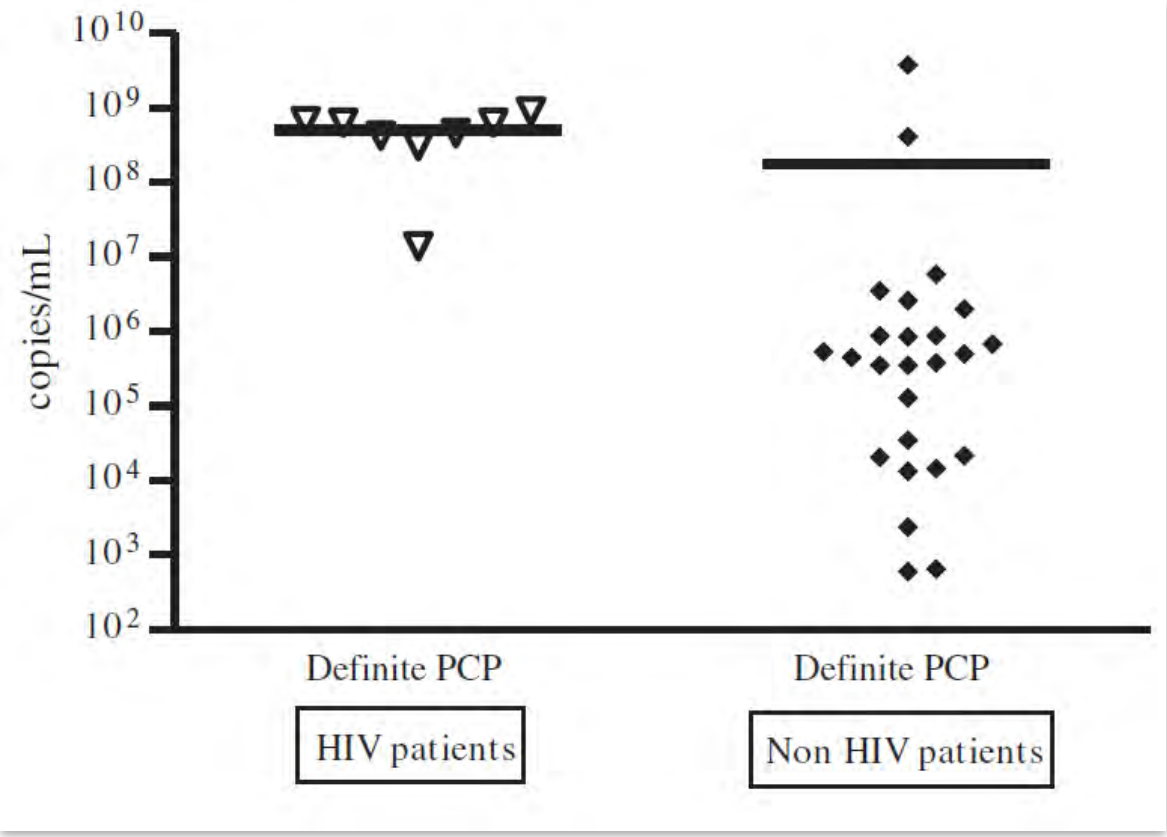
Clinical characteristics and laboratory results	Definite (n = 34)	Unlikely (n = 86)	*P* value
Age (mean)	58	56	0.18
Male sex (%)	27 (79%)	60 (70%)	0.2
Underlying disease			
HIV infection (%)	8 (23%)	0	<0.001
COPD (%)	4 (11%)	9 (10%)	1
Acute alcoholic hepatitis (%)	1 (2%)	9 (10%)	0.27
Others	3 (9%)	9 (10%)	
Corticosteroids	23 (67%)	71 (82%)	0.07
Other immunosuppressive agents	9 (26%)	41 (47%)	0.034
Anti-tumour chemotherapy	9 (26%)	16 (18%)	0.3
Mortality[a]	5 (15%)	3 (3%)	0.02
Positive DME (Giemsa)	14 (41%)	0	<0.001
Mean Ct value "in house" PCR[b] (SEM)	32 (0.8)	37 (0.25)	<0.001
Mean copy number/mL Bio-Evolution PCR[c] (SEM)	2.5×10^8 (1.2×10^8)	4.7×10^5 (1.4×10^5)	<0.001

PCR « maison » = PCR commerciale

Problématique de l'uniformisation et standardisation des techniques

Intérêt tout particulier pour le non-VIH

PCP et place de la PCR?



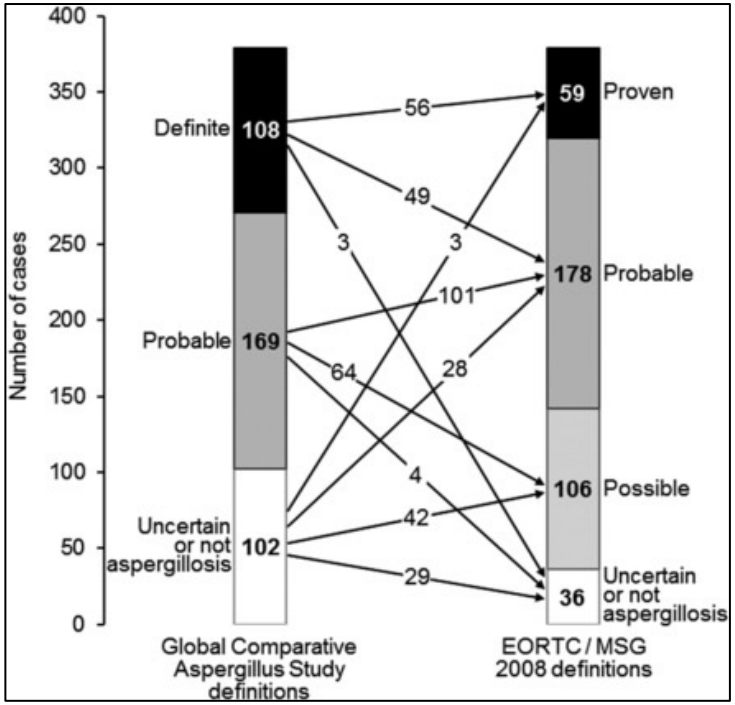
IF: Forme paucikystique du non VIH

PCR: CV VIH = CV Non VIH, donc intérêt en pratique clinique

Mais problématique du SEUIL

Traitement

Optimisation de la Catégorisation des API? Impact thérapeutique?



Application of the 2008 Definitions for Invasive Fungal Diseases to the Trial Comparing Voriconazole Versus Amphotericin B for Therapy of Invasive Aspergillosis: A Collaborative Study of the Mycoses Study Group (MSG 05) and the European Organization for Research and Treatment of Cancer Infectious Diseases Group.
Herbrecht, Raoul; Patterson, Thomas; Slavin, Monica; Marchetti, Oscar; Maertens, Johan; Johnson, Elizabeth; Schlamm, Haran; Donnelly, J; Pappas, Peter

Clinical Infectious Diseases. 60(5):713-720,

Table 2. Main Characteristics of the 343 Patients With a Possible, Probable, or Proven Invasive Aspergillosis After Recategorization

Characteristics	Voriconazole (n = 179)	Amphotericin B (n = 164)	*P* Value
Age, y, median (range)	42 (13–79)	52.5 (12–75)	.20
Sex, male, No. (%)	117 (65.4)	101 (61.6)	.50
Underlying condition, No. (%)			.69
Allogeneic HSCT	41 (22.9%)	34 (20.7)	
Autologous HSCT	11 (6.1)	8 (4.9)	
Acute myeloblastic leukemia	64 (35.8)	63 (38.4)	
Acute lymphoblastic leukemia	15 (8.4)	12 (7.3)	
Other hematologic malignancy	21 (11.7)	25 (15.2)	
Solid organ cancer	2 (1.1)	0	
Solid organ transplant	11 (6.1)	6 (3.7)	
Other nonmalignant disease*	14 (7.8)	16 (9.8)	
Neutropenia <500/μL	90 (50.3)	81 (49.4)	.91

Abbreviation: HSCT, hematopoietic stem cell transplant.

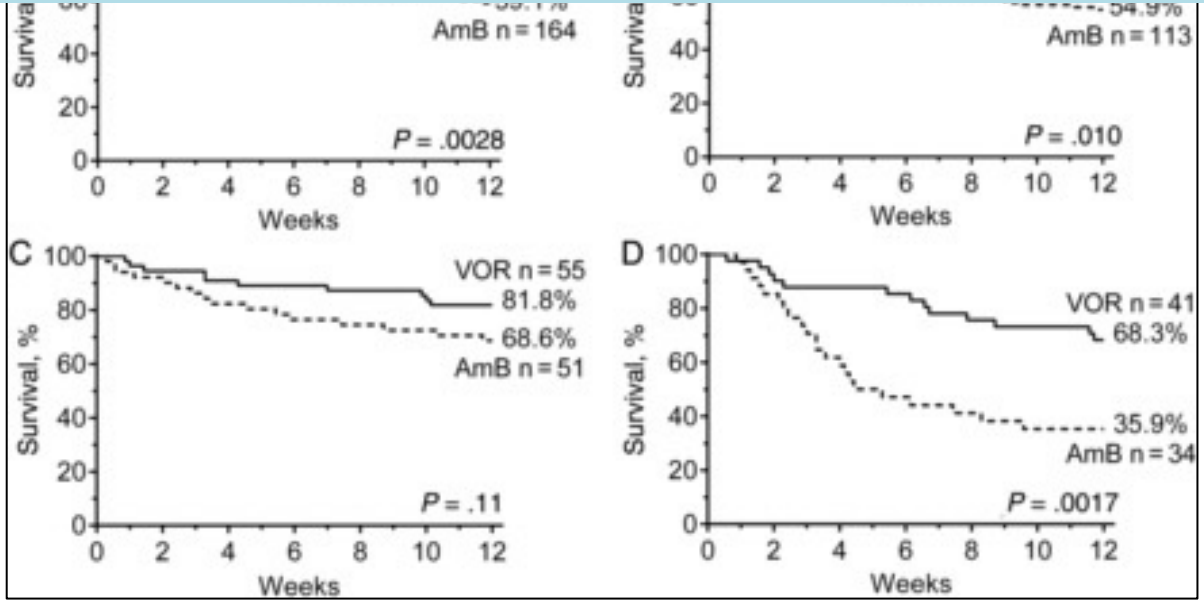
*Mostly high-dose steroid-treated or human immunodeficiency virus–positive patients.

Optimisation de la Catégorisation des API? Impact thérapeutique?

Table 4. Comparison of 12-Week Favorable Response and Survival Rates in the Original Global Comparative Aspergillus Study and After Recategorization According to Level of Certainty of Aspergillosis

Response	Possible Invasive Aspergillosis		Probable Invasive Aspergillosis		Proven (Definite) Invasive Aspergillosis		All Episodes of Invasive Aspergillosis	
	Original	Recategorization	Original	Recategorization	Original	Recategorization	Original	Recategorization
Response at week 12								
Voriconazole								
Favorable response, No./total (%)	NA	30/55 (65.5)	49/77 (64.7)	49/89 (55.1)	30/67 (44.8)	13/35 (37.1)	79/144 (52.9)	98/179 (54.7)
Amphotericin B								
Favorable response, No./total (%)	NA	20/51 (39.2)	34/92 (37.0)	23/89 (25.8)	8/41 (19.5)	6/24 (25.0)	42/133 (31.6)	49/164 (29.9)
Survival at week 12								
Voriconazole								

Meilleure catégorisation avec EORTC/MSG 2008
Efficacité supérieure du Voriconazole vs Amb
(quelque soit la catégorisation)



Traitement des Mucormycoses

Prospective pilot study of high-dose (10mg/Kg/day) liposomal amphotericin B (L-AMB) for the initial treatment of mucormycosis

Lanternier F et al. J Antimicrob Chemother. 2015; 70(11): 3116-23.

- 33 patients (Mucor mycose prouvée)
- 53% hémopathies
- 71% : traitement chirurgical
  - Réponse objective: 36% à S4, 45% à S12
- Mortalité: 38% S12, 53% S24 et S52
- Si Hémopathie: HR 3.15 (p: 0.002)
- Toxicité
  - 40% (16 patients): doublement de la créatinine
  - 10/16 retour à la normale en 12 semaines

Patients' characteristics	No. (%) or median (range)
Male	21 (62)
Age (years)	53 (0.50–78.10)
Time from symptom onset to treatment (days)	46 (4–344)
Underlying disease	
HM	18 (53)
haematopoietic stem cell transplant	5/18 (28)
GVHD	3/18 (17)
neutropenia	6/18 (33)
corticosteroids	8/18 (44)
DM	6 (18)
trauma	3 (9)
solid organ transplant	3 (9)
other[a]	4 (12)
Site of infection	
lung	10 (29)
rhino-orbito-cerebral	9 (26)
skin	6 (18)
disseminated	6 (18)

Mucormycose = Amphotericin B liposomal à 10mg/Kg/j + Abord chirurgical
Pronostic sombre
Efficacité et tolérance acceptables

Prophylaxie

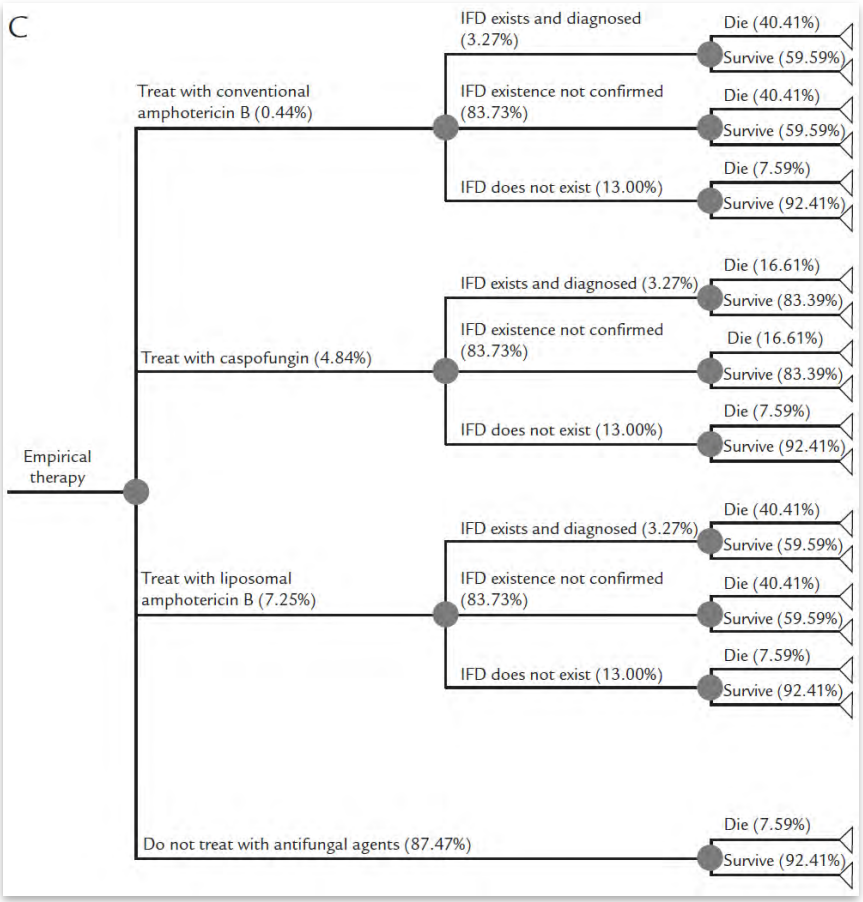
Stratégie empirique antifongique ou Expectative armée?

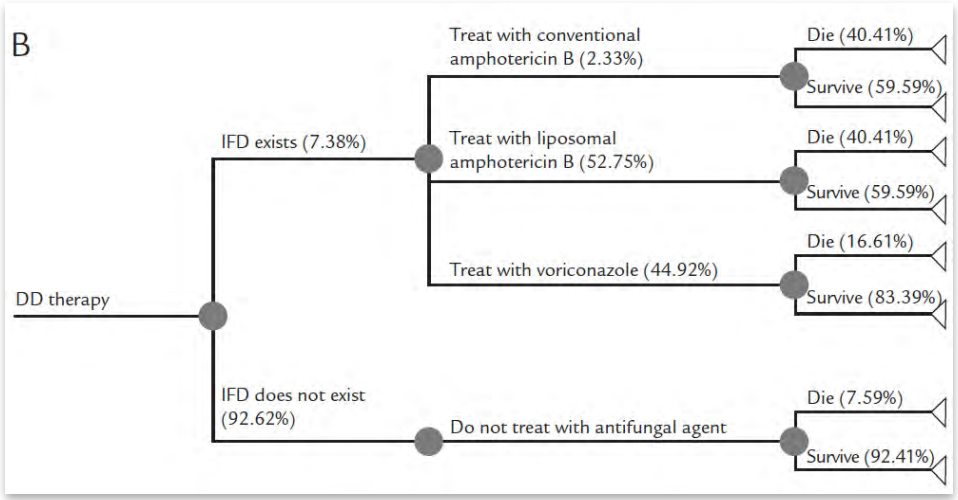
Clinical Therapeutics/Volume 37, Number 6, 2015

Economic Comparison of an Empirical Versus Diagnostic-Driven Strategy for Treating Invasive Fungal Disease in Immunocompromised Patients

Rosemary Barnes, MD[1]; Stephanie Earnshaw, PhD[2]; Raoul Herbrecht, MD[3];

- DD strategy dès que IFI suspectée (EORTC)
- Empirical strategy dès que neutropénie fébrile persistante après 48h d'ATB
  - Même sans argument pour IFI
- Amphotéricine B ou Amphotéricine B Liposomale ou Voriconazole

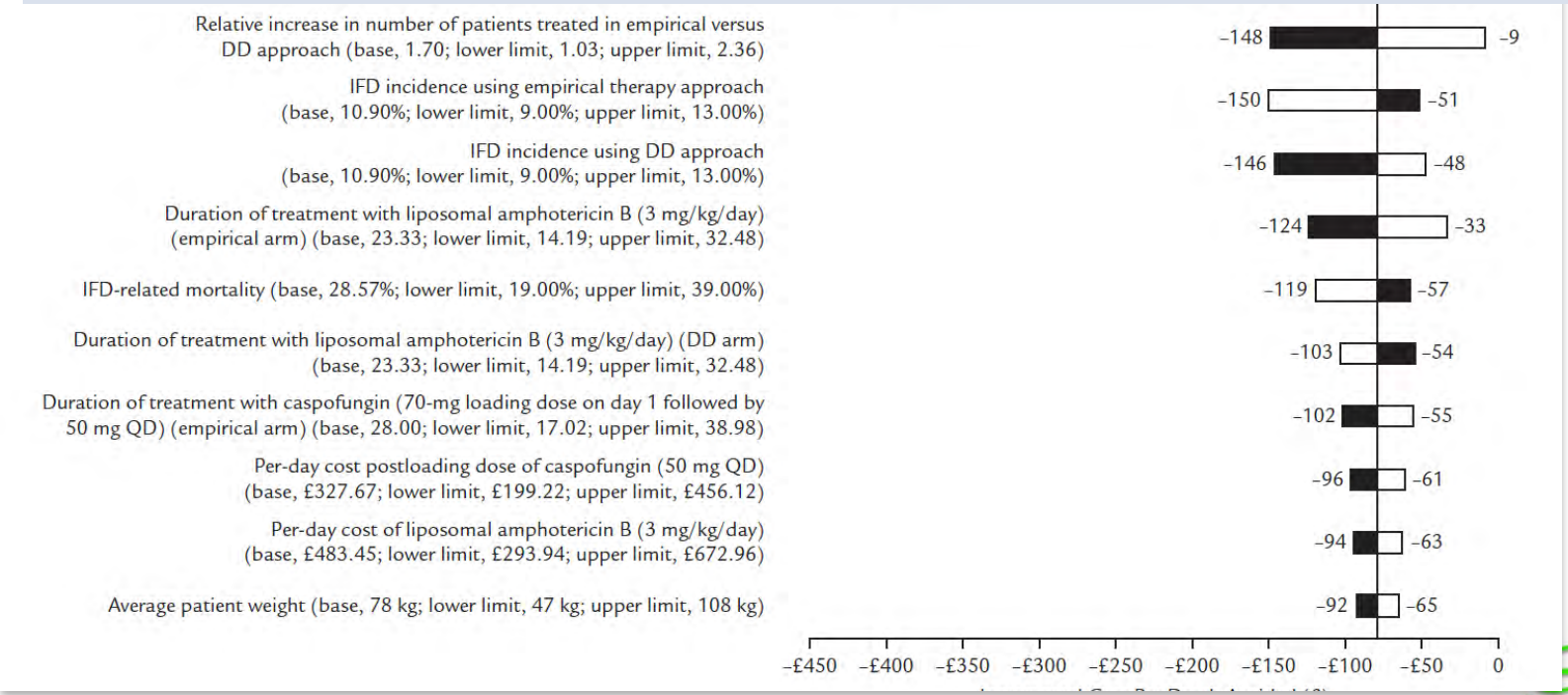




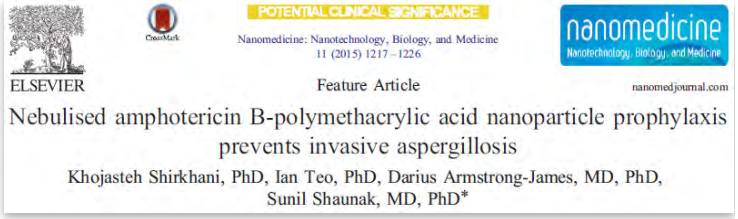
Stratégie empirique antifongique ou Expectative armée?

Model Outcome	DD Approach	Empirical Approach
Total costs, £ per patient	1561.29	2301.93
Antifungal treatment costs	799.21	1678.06
Antifungal agent AE costs	0.96	1.34
GM and PCR costs	27.46	0
Other medical costs*	733.66	622.53
No. of patients treated with antifungal drug therapy (per 1000 patients)	74	125
No. of diagnosed IFD (per 1000 patients)	74	33
No. of deaths (per 1000 patients)	92	102
Probability of survival, %	90.8	89.8

DD stratégie coût-efficace > Stratégie Empirique



Modalité novatrice de prophylaxie antifongique – Modèle murin


POTENTIAL CLINICAL SIGNIFICANCE

Nanomedicine: Nanotechnology, Biology, and Medicine
11 (2015) 1217–1226

nanomedicine
Nanotechnology, Biology, and Medicine

ELSEVIER

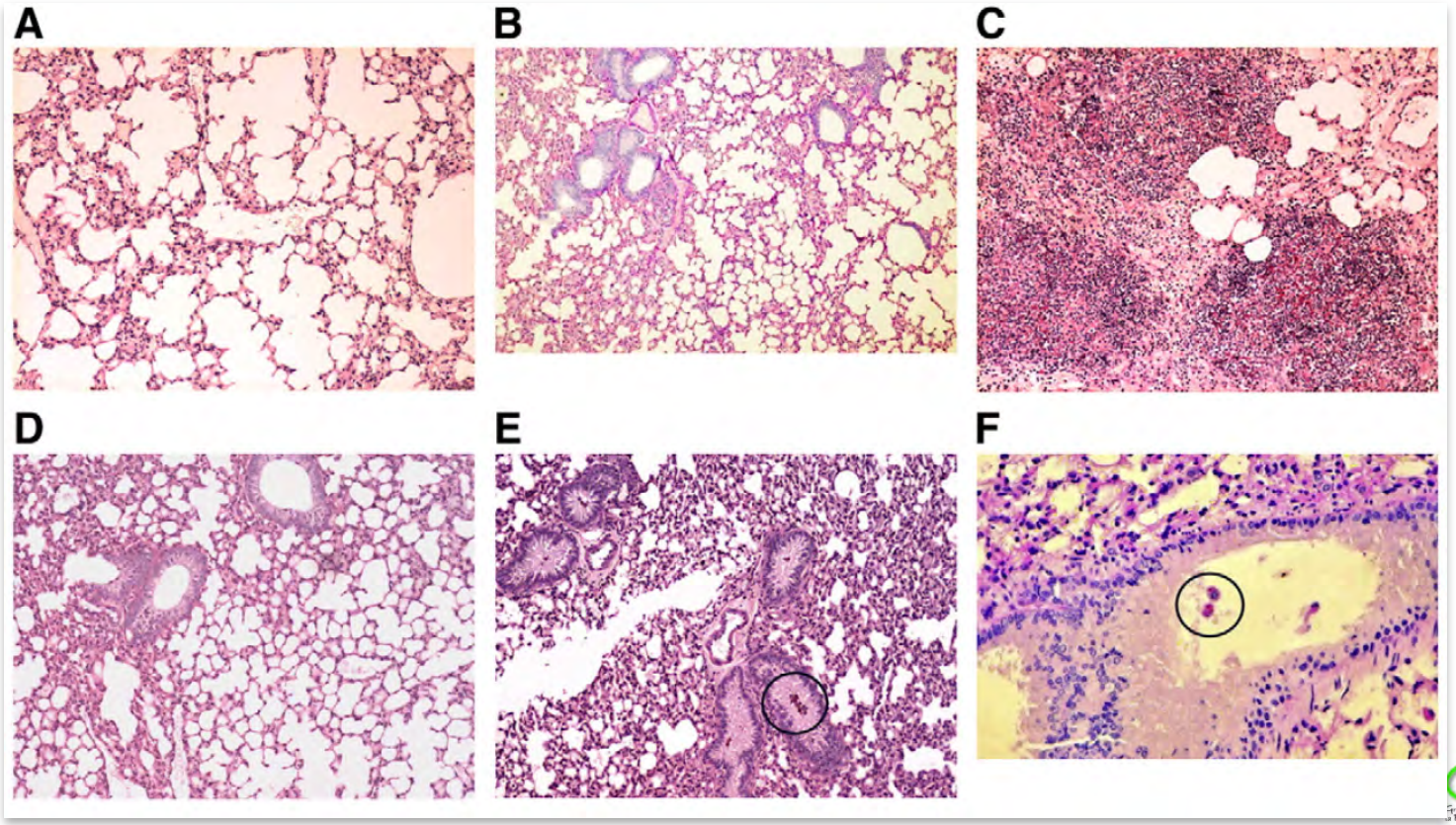
Feature Article

nanomedjournal.com

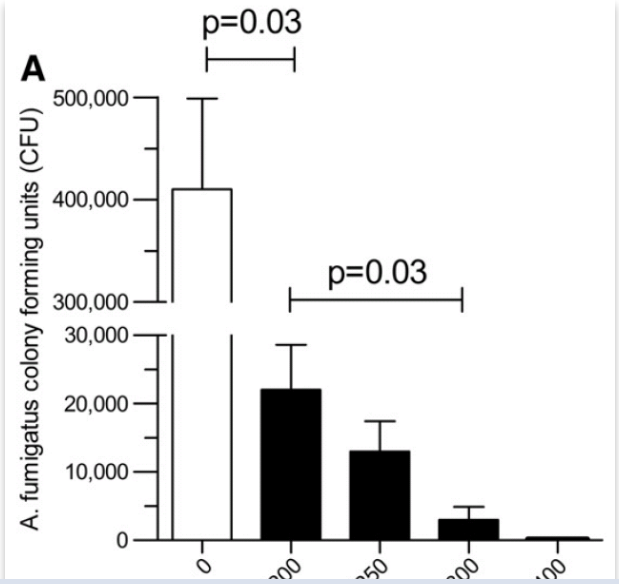
Nebulised amphotericin B-polymethacrylic acid nanoparticle prophylaxis prevents invasive aspergillosis

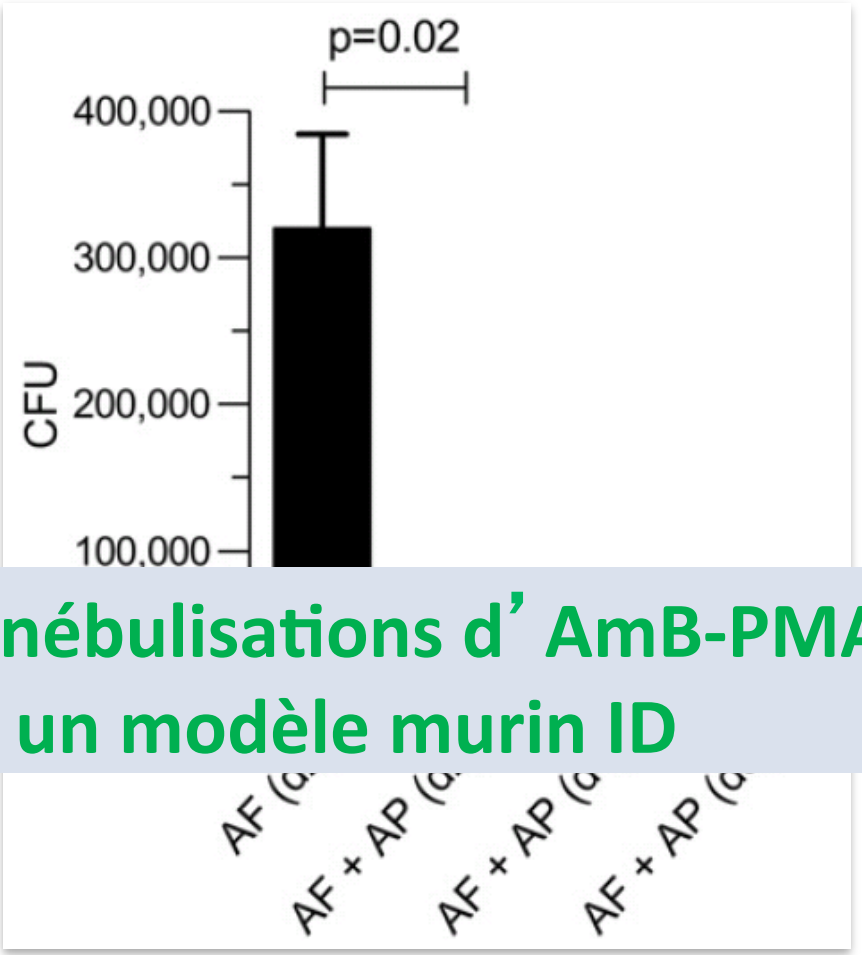
Khojasteh Shirkhani, PhD, Ian Teo, PhD, Darius Armstrong-James, MD, PhD, Sunil Shaunak, MD, PhD*

- Modèle murin (BALB/c et C57Bl/6)
  - Dexaméthasone et FK506
  - Instillation intra nasale de NaCl + spores d'A. fumigatus
  - Souris contrôle: instillation NaCl
  - Nébulisation de nanoparticules AmB-PMA

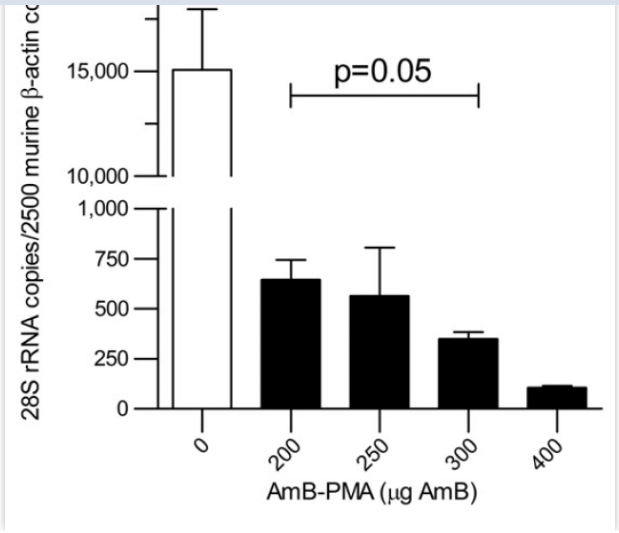


Modalité novatrice de prophylaxie antifongique – Modèle murin





Efficacité in vitro/vivo de nébulisations d'AmB-PMA en prophylaxie sur un modèle murin ID



Modalité novatrice de prophylaxie antifongique - clinique

- Etude randomisé, double aveugle contre placebo
- Nébulisation Amb-L (12.5mg)
  - 30 min - 2j consécutifs/7 jusqu'à PNN>500
- 139 patients Amb-L vs 132 patients placebo

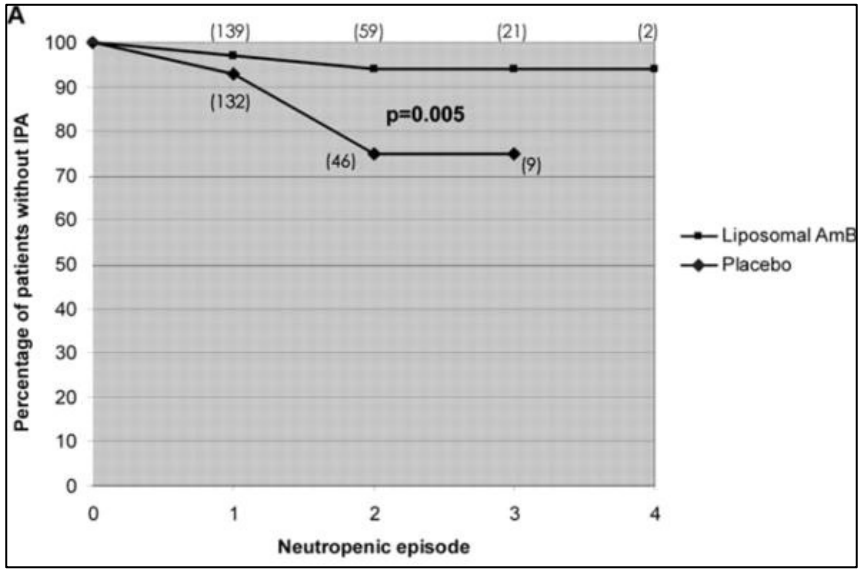
Aerosolized Liposomal Amphotericin B for the Prevention of Invasive Pulmonary Aspergillosis during Prolonged Neutropenia: A Randomized, Placebo-Controlled Trial. Rijnders, Bart; Cornelissen, Jan; Slobbe, Lennert; Becker, Martin; Doorduijn, Jeanette; Hop, Wim; Ruijgrok, Elisabeth; Luwenberg, Bob; Vulto, Arnold; Lugtenburg, Pieternella; de Marie, Siem

Clinical Infectious Diseases. 46(9):1401-1408, May 1, 2008. DOI : 10.1086/586739

Characteristics	Liposomal amphotericin B (n = 139)	Placebo (n = 132)	P
Age, mean years (range)	49 (18–73)	50 (20–74)	.64
Male sex/female sex	77/62	81/51	.33
HEPA filtration[a]	108	100	.77
Hematologic disease			
AML-MDS	65	67	.54
Other	74	65	
Hematologic treatment			
Chemotherapy	100	85	.19
Autologous HSCT	25	31	.29
Allogeneic HSCT	14	16	.70
Disease status			
Untreated	73	64	.54
Other[b]	66	68	
Treatment followed by allogeneic HSCT[c]	16	14	.85

NOTE. Data are no. of patients, unless otherwise indicated. AML, acute myeloid leukemia; HEPA, high-efficiency particulate air; HSCT, hematopoietic stem cell transplantation; MDS, myelodysplastic syndrome.

[a] Use of HEPA filtration of hospital room air during first course of chemotherapy.
[b] Partial remission, complete remission, refractory disease, or relapse.
[c] Inhalation therapy was not continued during allogeneic HSCT that followed intensive chemotherapy.



Voyage

Comment voyage l'« Immunodéprimé»?

INTERNAL MEDICINE JOURNAL

International travel in the immunocompromised patient: a cross-sectional survey of travel advice in 254 consecutive patients

C. Bialy,[1,2] K. Horne,[1,2] C. Dendle,[1,3] J. Kanellis,[2,3,4] G. Littlejohn,[2,5] I. Ratnam[1,6] and I. Woolley[1,2]

- 256 patients
  - 56 VIH - 100 transplantés rénaux - 100 connectivites sous IS
- Questionnaire
- 68% (105) ont voyagé depuis l'ID - Nb médian de voyages: 3

	HIV-positive	Renal transplant	Rheumatological condition	Overall
Participants	54	100	100	254
Immunocompromised at time of travel (*N*)	19 (35.2%)	42 (42.0%)	44 (44.0%)	105
Demographics				
Age (mean years)	54.4	49.38**	55.86	53.1
Male*	15 (78.9%)	20 (47.6%)	15 (34.1%)	50 (47.6%)
Australia as country of birth	9 (47.4%)	28 (66.7%)	26 (59.1%)	63 (60.0%)
English is primary language	17 (89.5%)	41 (97.6%)	38 (86.4%)	96 (91.4%)
Tertiary education	6 (31.6%)	19 (45.2%)	17 (38.6%)	42 (40.0%)
VFR traveller	12 (63.2%)	10 (23.8%)	19 (43.2%)	41 (39%)
High risk destination	12 (63.2%)	20 (47.6%)	25 (56.8%)	57 (54.3%)
Pre-travel advice (*n*)	10 (52.6%)	30 (71.4%)	32 (72.7%)	72 (68.6%)
Risk behaviour** (*n*/*N*)				
Food risk**	6/19 (31.6%)	10/35 (28.6%)	10/36 (27.8%)	69 (65.7%)
Sexual activity**	2/19 (10.5%)	1/35 (2.9%)	0/37	26 (28.9%)
Exposure to sharps**	0/19	3/35 (8.6%)	4/37 (10.8%)	3 (3.3%)
IVDU**	1/19 (5.3%)	0/35	0/37	7 (7.7%)
Tattoo**	1/19 (5.3%)	1/35 (2.7%)	1/37 (2.9%)	1 (1.0%)

«L'Immunodéprimé »: un voyageur comme les autres??
Point de vue Médical assurément différent du Patient

Conclusion

- Attirer **l'attention** sur certaines populations à risque
  - PCP et transplanté rénale (>2ans)/Connectivites
  - PCP et contamination inter humaine

- Modalités diagnostiques: **Biologie moléculaire**
  - Intérêt Diagnostique
  - Identification
  - Mais standardisation, seuil (PCP)…
  - Complément de techniques déjà utilisées (AGAS)

- Traitement/Prophylaxie
  - Meilleure catégorisation des IFI, sans réel impact TTT
  - **DD stratégie** > Stratégie empirique

- ID=**Globe trotteur**?

Merci de votre attention