Pneumocystose pulmonaire

Cours DES pneumologie
Ile de France
Phase socle

27/05/2021

Antoine Roux

(Hôpital Foch)

Introduction

PNEUMOCYSTIS CARINII—ETIOLOGIC AGENT OF INTERSTITIAL PLASMA CELL PNEUMONIA OF PREMATURE AND YOUNG INFANTS

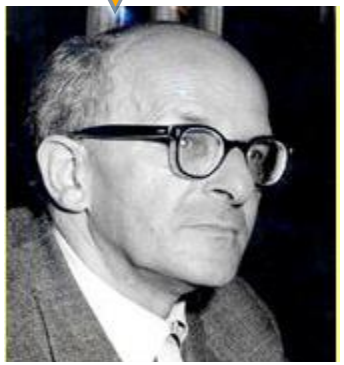
- Transplantation org solide
- Hémopathies malignes
- T solides
- Immunosuppression

Non VIH

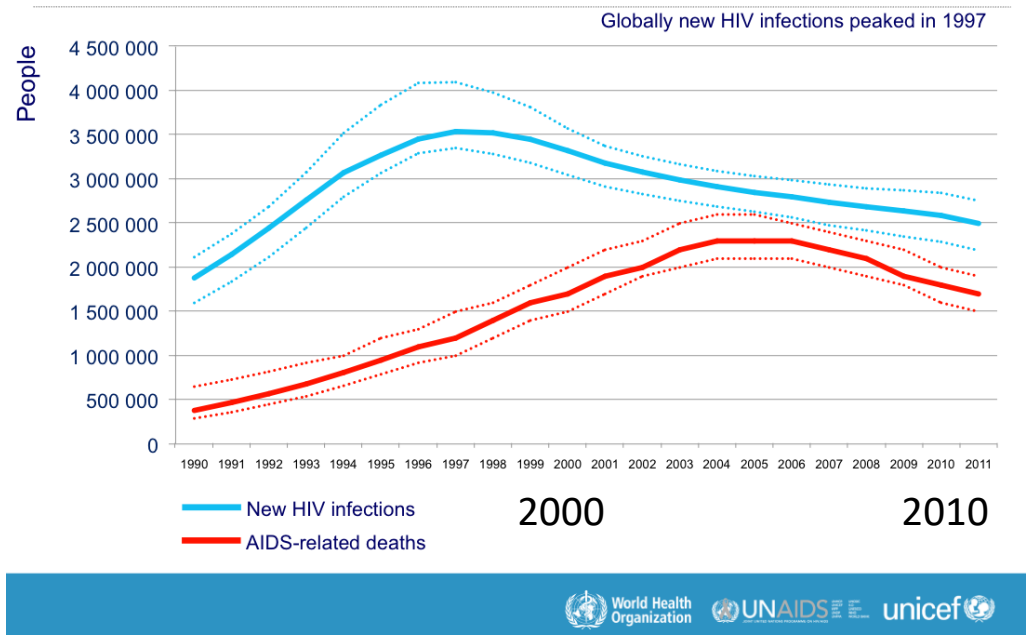
1909 — 1952 — Epidémie VIH

Antonio Carini

Vs. Chagas



Otto Jerovec



Pneumocystis jirovecii Disease: Basis for the Revised EORTC/MSGERC Invasive Fungal Disease Definitions in Individuals Without Human Immunodeficiency Virus *Lagrou, CID, 2021*

ECIL guidelines for the diagnosis of *Pneumocystis jirovecii* pneumonia in patients with haematological malignancies and stem cell transplant recipients *Alanio, J Antimicrob Chemother 2016*

Pneumocystis jiroveci in solid organ transplantation: Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice *Fishman, Clinical Transplantation, 2019*

***Pneumocystis jirovecii* Pneumonia in Patients with or without AIDS, France** *Roux, EID, 2014*

Présentations cliniques

Terrain
VIH vs. Non VIH

+

Clinique
non spécifique

+

Absence
de prophylaxie

Présentations cliniques

Terrain
VIH vs. Non VIH

Clinique
non spécifique

Absence
de prophylaxie

Particularités VIH vs. Non VIH

- Durée des symptômes plus courte pour non VIH (#4-5jrs vs. 21jrs)
- Non VIH plus graves au diagnostic:
  - Admission en réa (35% vs. 50%)
  - VNI (8% vs. 16%)
  - VM (11% vs. 30%)
  - Choc (2 vs. 7%)
- Début du traitement plus tardif pour non VIH

Roux, EID, 2014

Présentations cliniques

Terrain
VIH vs. Non VIH

+

Clinique non spécifique

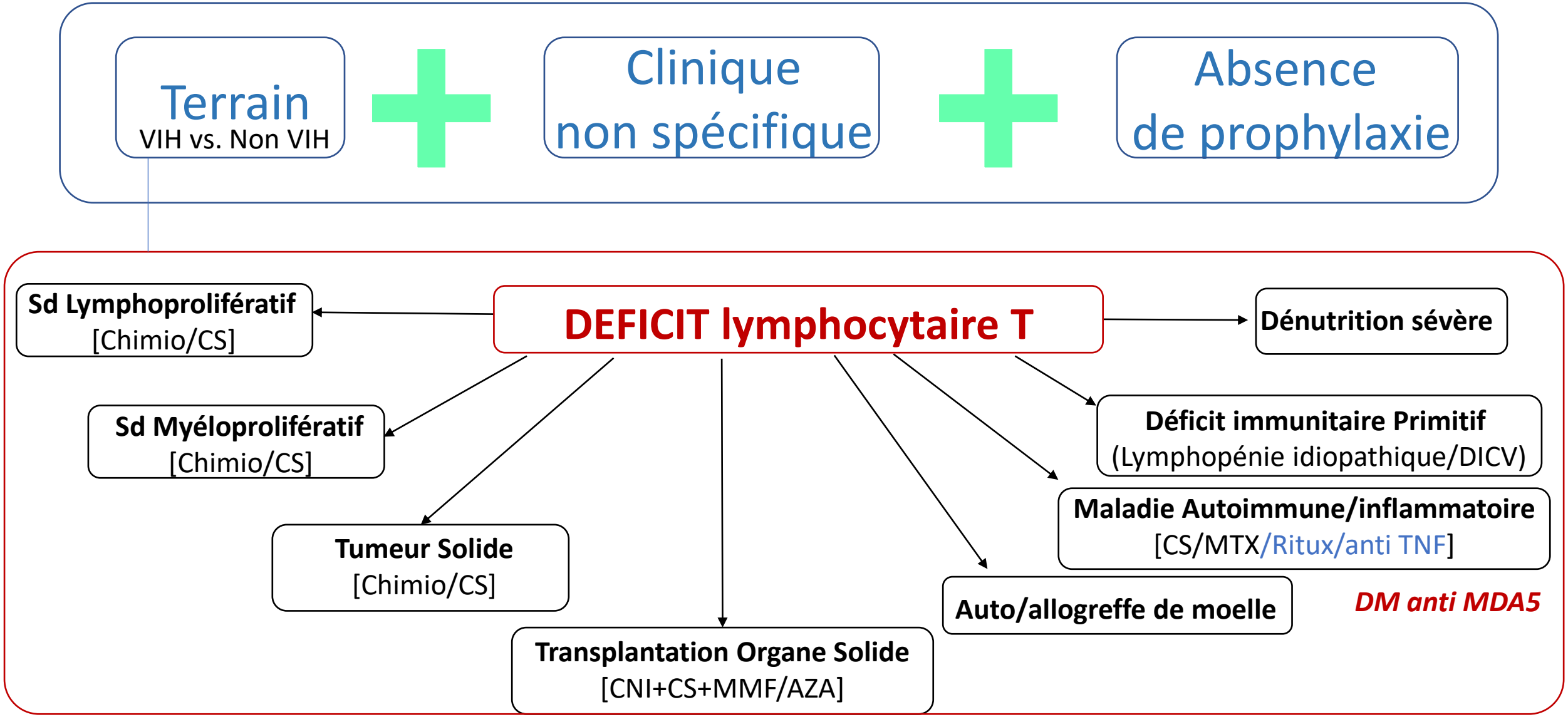
+

Absence de prophylaxie

Host factors	• Use of therapeutic doses of ≥0.3 mg/kg prednisone equivalent for ≥2 weeks in the past 60 days • Low CD4+ lymphocyte counts (observed or expected; <200 cells/mm^3) induced by a medical condition, anticancer, anti-inflammatory, and immunosuppressive treatment, including but not limited to: - Primary immunodeficiencies with numeric/functional T-cell deficiency - Acute leukemia, non-Hodgkin's lymphoma, solid tumors, allogeneic HSCT - Solid-organ transplantation - Autoimmune- and hyperinflammatory disorders, including treatment with agents that lead to functional T-cell deficiencies

Lagrou, CID, 2021

Présentations cliniques



Présentations cliniques

Terrain
VIH vs. Non VIH

Clinique
non spécifique

Absence
de prophylaxie

Incidence: 0.1 >> 10%

Incidence de pneumocystose pulmonaire chez les patients d'oncologie en fonction

Incidence de la pneumocystose pulmonaire chez des transplantés d'organe en l'absence de

Organ transp

Kidney
Liver
Heart
Heart-lung/l

Incidence de la pneumocystose pulmonaire au cours de différentes pathologies auto-immunes ou inflammatoires

Dis

Lym
Acu
Othe
Soli
Brai
Allo

Gra
Peri
Poly
Sys
Rhe

Drug	Action	PJP incidence (%)
Infliximab (Remicade®)	Anti-TNF α	0.3
Etanercept (Embrel®)	Anti-TNF α	0.1
Adalimumab (Humira®)	Anti-TNF α	0.3
Tocilizumab (RoActemra®)	Anti IL6	0.2
Abatacept (Orencia®)	Anti CD 28	0.1

Présentations cliniques

Terrain
VIH vs. Non VIH

Clinique non spécifique

Absence de prophylaxie

Clinical criteria	• Fever • Respiratory symptoms including cough, dyspnea, or hypoxemia • Bilateral or diffuse GGO on X-ray with interstitial infiltrates as the predominant feature; alveolar, alveolar-interstitial, and unilateral infiltrates are less frequent • Extensive, mostly diffuse GGO on CT scans, which typically has an upper lobe and perihilar predominance, sometimes with peripheral sparing or a mosaic pattern; consolidations, small nodules, and unilateral infiltrates are less frequent

Lagrou, CID, 2021

- Toux (8-70%)/DE (24-80%)/F°(50-80%)
- Crépitants/normale (20%)
- AA➔02➔ SDRA
- Choc: autre infection

Présentations cliniques

Terrain
VIH vs. Non VIH

+

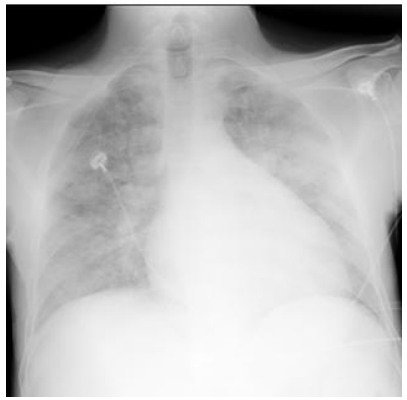
Clinique non spécifique

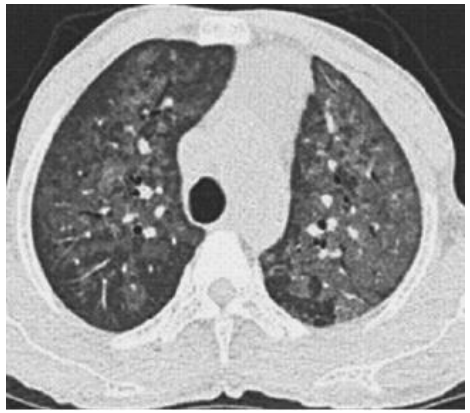
+

Absence de prophylaxie

Radio de thorax

- Atteinte alvéolo-interstielle
- peri hilaire
- « Normale » (20-30%)





TDM thoracique

Le plus fréquent

- Verre dépoli,
- Diffus, prédominance apicale
- bilatéral
- « crazy paving »
- (Fibrose)

Rares mais « classiques »

- Kystes (VIH>>non VIH)
- pneumothorax
- Séquelle Fibrose
- (Nodules)

PCP pas le premier Dg si

- Condensations
- Micronodules
- Nodules

Présentations cliniques

Terrain
VIH vs. Non VIH

+

Clinique non spécifique

+

Absence de prophylaxie

Radio de thorax

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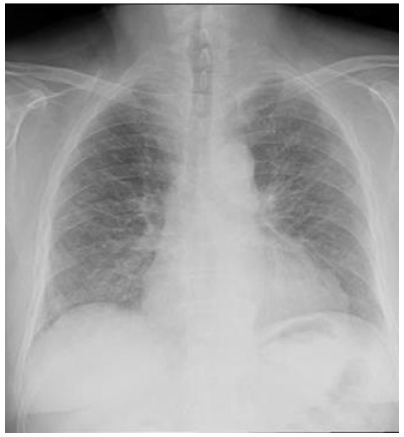

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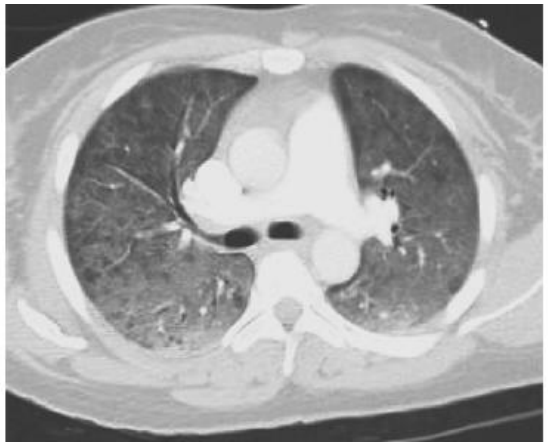

PCP pas le premier Dg si

- Condensations
- Micronodules
- Nodules

Diagnostic

Terrain
VIH vs. Non VIH

+

Clinique
non spécifique

+

Absence
de prophylaxie

1/ évoquer le Diagnostic

2/ gamme diagnostique

- Infections chez TOS
- VD chez ID: infection vs. non infection

Infection in Solid-Organ Transplant Recipients

Common Infections in Solid-Organ Transplant Recipients

<1 Month	1–6 Months	>6 Months
Infection with antimicrobial-resistant species: MRSA VRE Candida species (non-albicans) Aspiration Catheter infection Wound infection Anastomotic leaks and ischemia *Clostridium difficile* colitis Donor-derived infection (uncommon): HSV, LCMV, rhabdovirus (rabies), West Nile virus, HIV, *Trypanosoma cruzi* Recipient-derived infection (colonization): Aspergillus, pseudomonas	With PCP and antiviral (CMV,HBV) prophylaxis: Polyomavirus BK infection, nephropathy *C. difficile* colitis HCV infection Adenovirus infection, influenza *Cryptococcus neoformans* infection *Mycobacterium tuberculosis* infection Anastomotic complications Without prophylaxis: Pneumocystis Infection with herpesviruses (HSV, VZV, CMV, EBV) HBV infection Infection with listeria, nocardia, toxoplasma, strongyloides, leishmania, *T. cruzi*	Community-acquired pneumonia, urinary tract infection Infection with aspergillus, atypical molds, mucor species Infection with nocardia, rhodococcus species Late viral infections: CMV infection (colitis and retinitis) Hepatitis (HBV, HCV) HSV encephalitis Community-acquired (SARS, West Nile virus infection) JC polyomavirus infection (PML) Skin cancer, lymphoma (PTLD)

Fishman, NEJM 2007

F, 56 ans, Emphysème , Crohn sous Anti TNF puis Vedolizumab

Hyperimmunisée pré op: PLEX+ Ritux+ IGIV

TP le 02/12/20 Induction SIMULECT

Rejet cellulaire
M3
M9
M12

Immunosuppression:
MMF>> AZA

Prophylaxie:
BF>> Atovaquone

1 Tacrolimus (ADOPORT°) non substituable, MTE 3,5mg le matin et 3 mg le soir (objectif : résiduelle entre 8 et 10ng/ml)SUBLINGUAL
2 Azathioprine (Imurel°), non substituable, MTE 75 mg le matin PO
3 Prednisone (CORTANCYL°) 5mg PO
4 Sulfamethoxazole - Trimethoprime (BACTRIM° fort) 800 mg SUSPENDU PO
5 Wellvone 750mg x2/jour PO
6 Folate 5 mg 1 comp/jour PO
7 Calcium (CACIT°) vit D3 500mg/440UI 2 cp par jour PO
8 Deroxat 20mg par jour PO
9 Colecalciferol (UVEDOSE°) 100000 UI 1 ampoule x2/mois PO
10 Kayexalate 1 CAM /J PO
11 Mag 2 100mg 1 cp matin et 1 cp soir pendant 10 jours uniquement en cas de crampes PO
12 Domperidone (MOTILIUM°) 10mg 1 cp x3 par jour 15 minutes avant les repas PO
13 Métoclopramide (PRIMPERAN°) 10mg 1 comprimé toutes les 8 heures si nausée
14 Lansoprazole (LANZOR°) 30 mg x2 par jour PO
15 Macrogol (MOVICOL°) 2 Sachets par jour si ralentissement du transit PO
16 Acétate de flécaïnide (FLECAINE LP°) 100 mg 1cp/j PO
17 Bisoprolol 2,5 mg 1 cp matin et soir PO
18 Apixaban (ELIQUIS) 5mg x2/jour à suspendre 48heures avant les BTB PO
19 Paracetamol (DOLIPRANE°) 1000mg x3 par jour si douleurs PO
20 Lidocaïne emplatre (Versatis°) 1 patch/jour cut
21 Acide zolédronique 5 mg (ACLASTA°) 1 injection en juillet en rhumato à Amiens IVL
22 VEDOLIZUMAB 300mg : 1 injection mensuelle à Amiens IV
23 Darbepoietine 20µg tout les 15jrs SC
24 Valaciclovir 1000mg x2/jour PO

F, 56 ans, Emphysème , Crohn sous Anti TNF puis Vedolizumab

Hyperimmunisée pré op: PLEX+ Ritux+ IGIV

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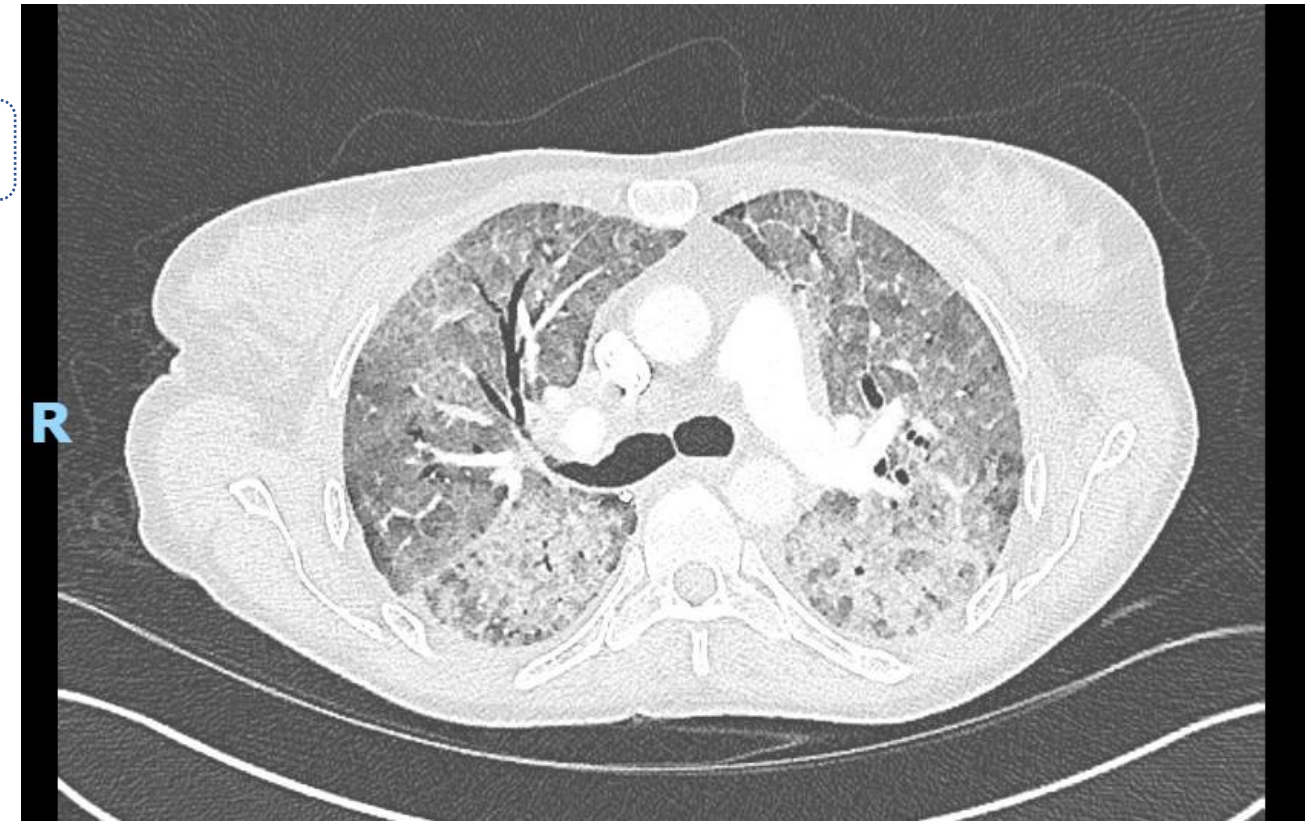
Rejet cellulaire
M3
M9
M12

Immunosuppression:
MMF>> AZA

Prophylaxie:
BF>> Atovaquone



08/2022
F°+ Toux+ DE + baisse spiromètre

TDM thorax+ LBA + Sd inflam biologique
Bactério:
Virus: COVID, CMV, autres
Myco: PCP

F, 56 ans, Emphysème , Crohn sous Anti TNF puis Vedolizumab

Hyperimmunisée pré op: PLEX+ Ritux+ IGIV

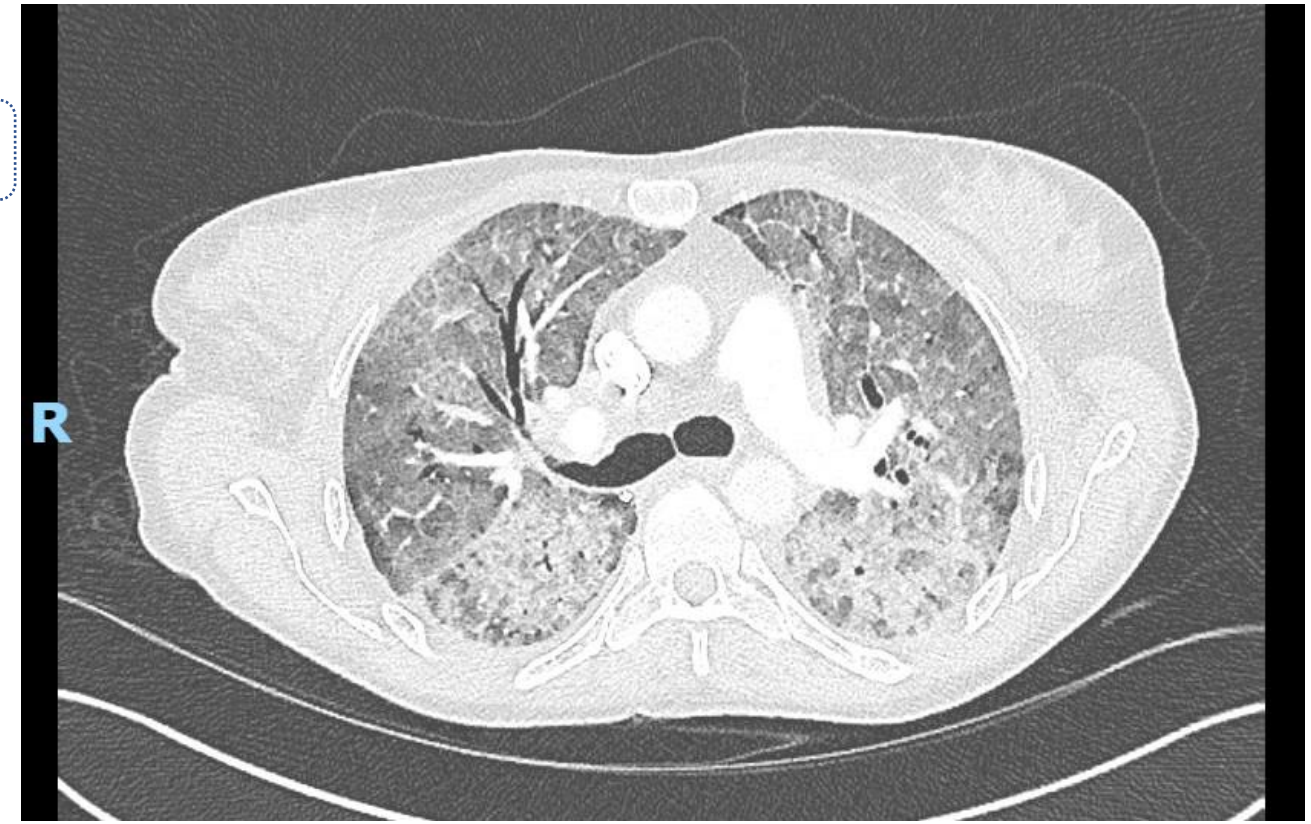
TP le 02/12/20 Induction SIMULECT

Rejet cellulaire
M3
M9
M12

Immunosuppression:
MMF>> AZA

Prophylaxie:
BF>> Atovaquone

Ulcération linguale (HSV)
>> stop Atovaquone



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F, 56 ans, Emphysème , Crohn sous Anti TNF puis Vedolizumab

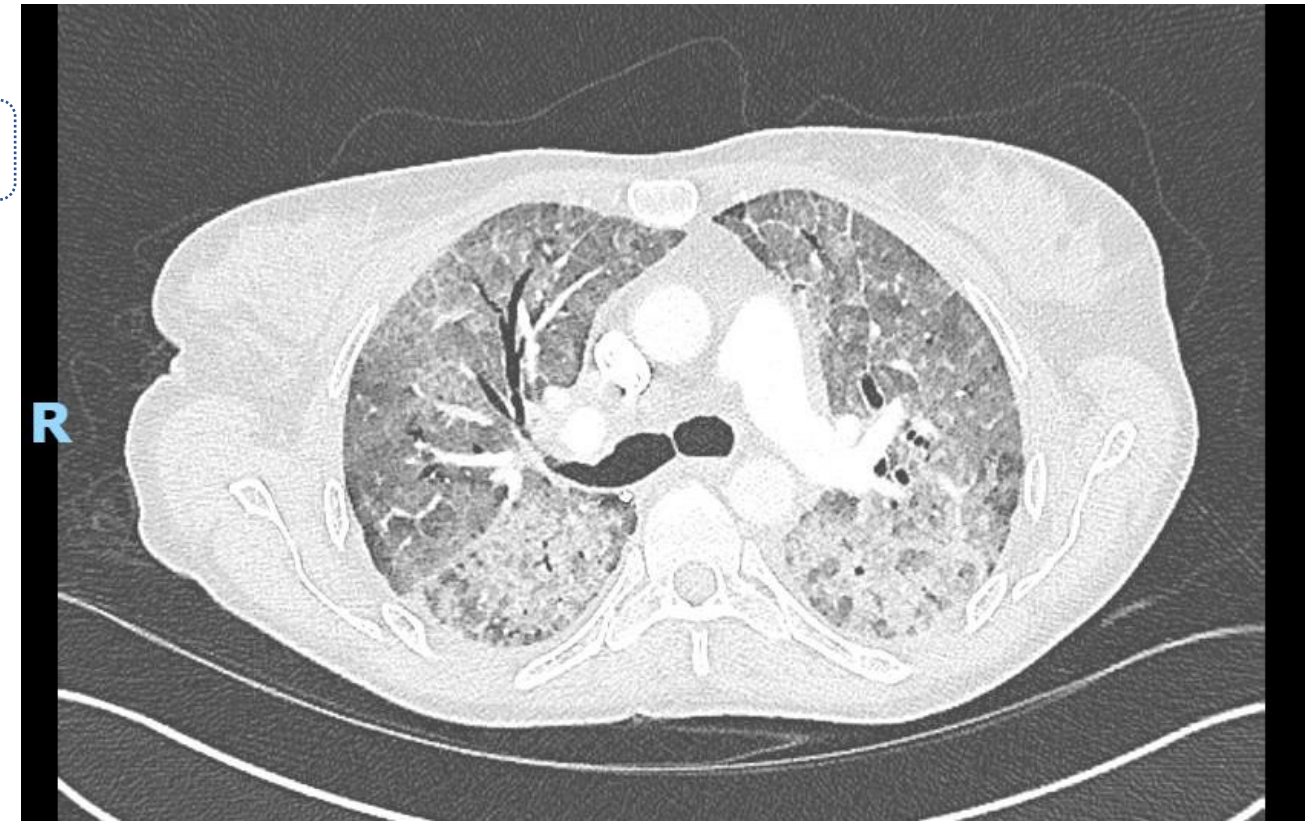
Hyperimmunisée pré op: PLEX+ Ritux+ IGIV

TP le 02/12/20 Induction SIMULECT

Rejet cellulaire
M3
M9
M12

Immunosuppression:
MMF>> AZA

Prophylaxie:
BF>> Atovaquone



08/2022
F°+ Toux+ DE + baisse spiromètre
+diarrhée/dlr abdo

TDM thorax+ LBA + Sd inflam biologique
Bactério:
Virus: COVID, **CMV**, autres
Myco: PCP

Diagnostic

Terrain
VIH vs. Non VIH

+

Clinique
non spécifique

+

Absence
de prophylaxie

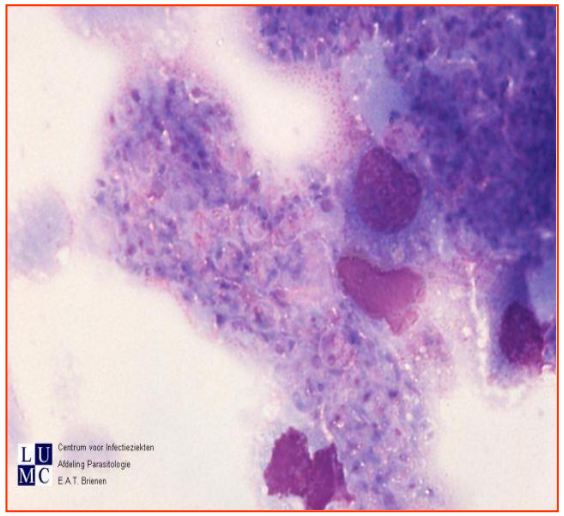
1/ évoquer le Diagnostic
2/ gamme diagnostique
3/ documentation microbiologique
(patient avec Dg ont un meilleur pronostic)

Diagnostic microbiologique

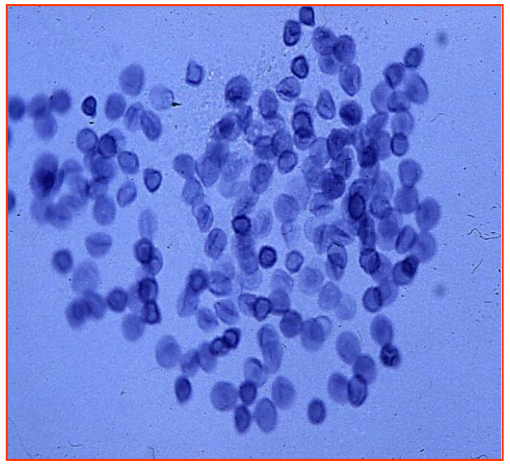
Prélèvements

- LBA+++
- Expectorations induites

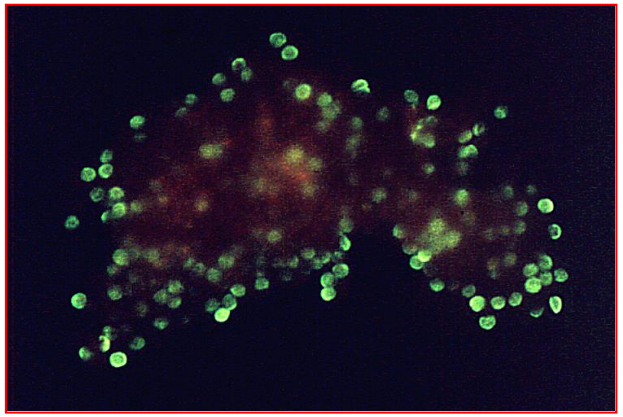
Colorations Classiques= MGG



Colorations Spécifiques= Grocott/ BTO



Immunofluorescence

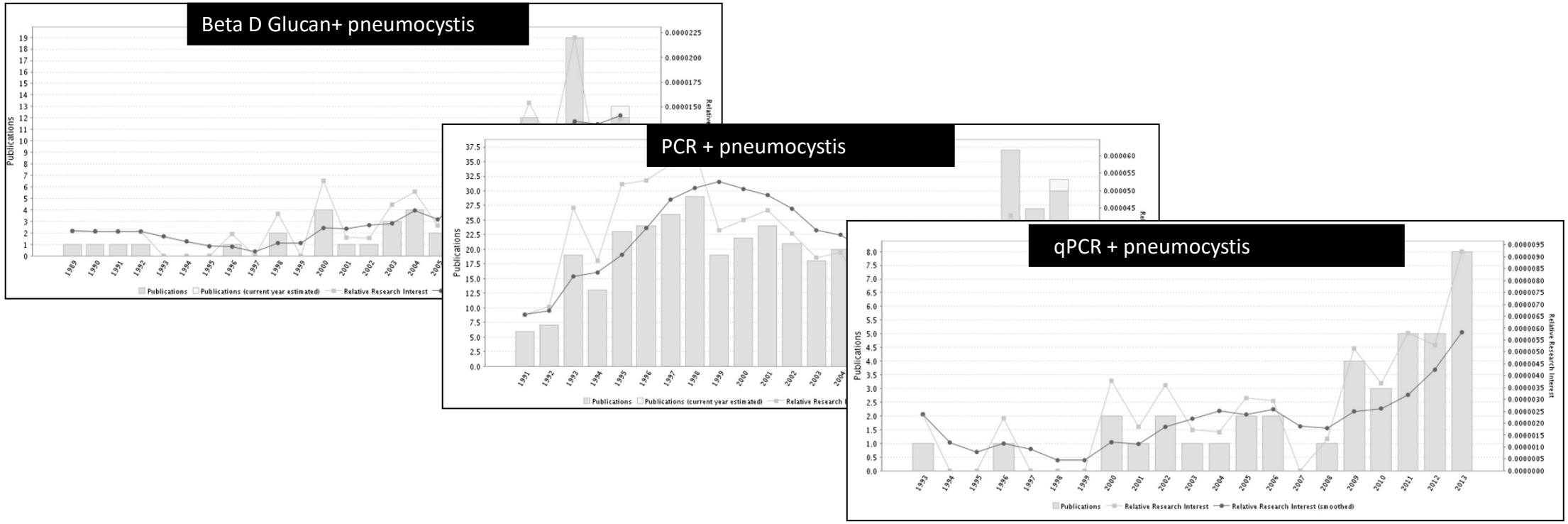


Performance diagnostique des Techniques classiques

- Suffisant pour VIH
- Insuffisant pour non VIH (formes paucikystiques)

« nouveaux outils »: qPCR et betaD glucan

1° publications➔ BDG= 1989/ PCR= 1991/ PCRq= 1993-96



« Nouveaux outils »: qPCR

- qPCR
- Cible
- Seuil (double seuil/zone grise)
- Standardisation
- Faux négatif
- LBA vs. Non invasif

- Permet ***quantification*** de la charge fongique
- gène glycoprotéine de surface/ sous unité ribosomale
  - Mitochondrial large-subunit ribosomal RNA (mtLSU)
  - Mitochondrial small-subunit ribosomal RNA (mtSSU)
  - 18S ribosomal RNA
  - internal transcribed spacer (ITS)
  - 5S rRNA
  - DHPS,
  - B-tubulin,
  - HSP70
- ***Capacité de détection***+++ ➔ permet détection sur prvlts non invasifs

« Nouveaux outils »: qPCR

- qPCR
- Cible
- Seuil (double seuil/zone grise)
- Standardisation
- Faux négatif
- LBA vs. Non invasif

Intérêt de la VPN
PCR+ >>> différencier colonisation/maladie

"thresholds": a "high" threshold that would diagnose PCP with 100% specificity and a "low" threshold that would exclude PCR with a high degree of certainty (eg, where PCR is performed on BAL fluid). Inevitably, there will be patients with results in the gray zone in-between the 2 thresholds. Therefore, these results should be interpreted in the context of the patient's underlying disease, immunosuppressive therapies, and other treatments to inform decisions of whether or not to institute

Lagrou, CID, 2021

« Nouveaux outils »: qPCR

- qPCR
- Cible
- Seuil (double seuil/zone grise)
- **Standardisation**
- Faux négatif
- LBA vs. Non invasif

The *Pneumocystis* Working Party of the Fungal PCR Initiative (www.fpcri.eu) has been working towards such a consensus method. A 16-laboratory international study confirmed the large (10 000-fold) variation between qPCR assays for a given sample.

However, test variability observed due to master mix and thermocycler parameters prevented the application of a consensual threshold and test standardization is essential [73].

Lagrou, CID, 2021

« Nouveaux outils »: qPCR

- qPCR
- Cible
- Standardisation
- Seuil (double seuil/zone grise)
- **Faux négatif**
- LBA vs. Non invasif

A misleading false-negative result of *Pneumocystis* real-time PCR assay due to a rare punctual mutation: A French multicenter study

- unreported mutation at position 210 (C210T) of the mitochondrial
- large subunit ribosomal RNA (mtLSUrRNA)
- Fce= 0.28%
- This low frequency should not call into question the routine use of this PCR assay
- the occurrence of the false-negative PCR result provides arguments for maintaining microscopic techniques combined to PCR assays to achieve PCP diagnosis

Le Gal, Med Mycology, 2016

« Nouveaux outils »: qPCR

- qPCR
- Cible
- Standardisation
- Seuil (double seuil/zone grise)
- Faux négatif
- **LBA vs. Non invasif**

•Expectoration induite
•Ecouvillon rhinopharyngé

•Aspiration rhinopharyngé
•Lavage oro pharyngé

•Accessibilité
•Rapidité exécution
•Moindre dangerosité*
•Autres recherches (virologie/germes intracellulaires)
•Réduction des couts
•Perd information sur cellularité LBA/diagnostic différentiel
• ⚠ 20-30% de co infection ⚠

« Nouveaux outils »: qPCR

- qPCR
- Cible
- Standardisation
- Seuil (double seuil/zone grise)
- Faux négatif
- **LBA vs. Non invasif**

Elie vs. Azoulay

Diagnosis and outcome of acute respiratory failure in immunocompromised patients after bronchoscopy *Bauer, ERJ, 2019*

Multi national, prospective EFRAIM study

Pronostic [NIT+Fibro] vs. [NIT]

Propensity score

[NIT+Fibro] plus graves

- Plus de diagnostic dans [NIT+Fibro]
- Plus d'intubation dans [NIT+Fibro] (86 vs.43)
- Plus de mortalité dans [NIT+Fibro] 49%vs.41% (OR 1,3-1,5)

Diagnostic Strategy for Hematology and Oncology Patients with Acute Respiratory Failure
Randomized Controlled Trial *Azoulay, AJRCCM, 2010*

» FO-BAL performed in the intensive care unit did not significantly increase intubation requirements in critically ill cancer patients with ARF. Noninvasive testing alone was not inferior to noninvasive testing plus FO-BAL for identifying the cause of ARF. »

« Nouveaux outils »: beta D Glucan

- **Seuil (double seuil)**
- **VPN>>> pour Dg de PCP**
- **VPP>>> pour différencier colo/Dg**
- Non SP >> autres IFI
- Faux positifs
- Faux négatifs
- Pas de test unitaire
- Délai pour Dg

Clinical Performance of (1,3) Beta-D Glucan for the Diagnosis of *Pneumocystis* Pneumonia (PCP) in Cancer Patients Tested With PCP Polymerase Chain Reaction

80pg/mL threshold

Table 3. Beta-D Glucan Performance at 80 pg/mL Threshold in All *Pneumocystis* Pneumonia Polymerase Chain Reaction Patients

	PCP PCR +	PCP PCR –
BDG + (>80 pg/mL)	37	70
BDG – (<80 pg/mL)	16	315
Total	53	385
Sensitivity	69.8%	95% CI (56.5–80.5%)
Specificity	81.2%	95% CI (77.7–85.4%)
PPV	34.6%	95% CI (26.2–44.0%)
NPV	95.2%	95% CI (92.3–97.0%)

Table 5. Beta-D Glucan Performance at 80 pg/mL Threshold in *Pneumocystis* Pneumonia Polymerase Chain Reaction–Positive Patients

	Definite/Probable PCP	Possible PCP
BDG + (>80 pg/mL)	35	2
BDG – (<80 pg/mL)	5	11
Total	40	13
Sensitivity	87.5%	95% CI (73.2–95.8%)
Specificity	84.6%	95% CI (54.6–98.1%)
PPV	94.6%	95% CI (81.8–99.3%)
NPV	68.8%	95% CI (41.3–89.0%)

200pg/mL threshold

Table 4. Beta-D Glucan Performance at 200 pg/mL Threshold in All *Pneumocystis* Pneumonia Polymerase Chain Reaction Patients

	PCP PCR +	PCP PCR -
BDG + (>200 pg/mL)	28	37
BDG – (<200 pg/mL)	25	348
Total	53	385
Sensitivity	52.8%	95% CI (38.6–66.7%)
Specificity	90.4%	95% CI (87.0–93.1%)
PPV	43.9%	95% CI (31.7–56.7%)
NPV	93.3%	95% CI (90.3–95.6%)

Table 6. Beta-D Glucan Performance at 200 pg/mL Threshold in *Pneumocystis* Pneumonia Polymerase Chain Reaction–Positive Patients

	Definite/Probable PCP	Possible PCP
BDG + (>200 pg/mL)	28	0
BDG – (<200 pg/mL)	12	13
Total	40	13
Sensitivity	70.0%	95% CI (53.5–83.4%)
Specificity	100.0%	95% CI (75.3–100.0%)
PPV	100.0%	95% CI (87.7–100.0%)
NPV	52.0%	95% CI (31.3–72.2%)

<80pg/mL: VPN=95%
80-200: zone grise
>200pg/mL: VPP=100%.

Manque Proba pre test

Morjaria. , CID, 2019

« Nouveaux outils »: beta D Glucan

- **Seuil (double seuil)**
- **VPN>>> pour Dg de PCP**
- **VPP>>> pour différencier colo/Dg**
- Non SP >> autres IFI
- Faux positifs
- Faux négatifs
- Pas de test unitaire
- Délai pour Dg

Diagnostic accuracy of serum (1-3)-β-D-glucan for *Pneumocystis jirovecii* pneumonia: a systematic review and meta-analysis

347>>>> 23 études inclues

	VIH	Non VIH
Sensibilité	0.94 (0.91-0.96)	0.86 (0.78-0.91)
Spécificité	0.83 (0.69-0.92)	0.83 (0.72-0.90)

Conversely, a negative BDG test to 'rule out' PJP with 95% certainty (post-test probability of 5%) requires that the pre-test probability be low (<20%). Therefore, for low-risk non-HIV populations, the principal role of the BDG assay would be to exclude PJP, and most positive tests will require further investigation.

Probabilité pré TEST non évaluée++++

Del Corpo,CM&I, 2020

« Nouveaux outils »: beta D Glucan

- Seuil (double seuil)
- VPN>>> pour Dg de PCP
- VPP>>> pour différencier colo/Dg
- **Non SP >> autres IFI**
- **Faux positifs**
- Faux négatifs
- Pas de test unitaire
- Délai pour Dg

Infectious
-Other fungall infection
In HIV patient: Cryptococcosis (rarely positive), histoplasmosis, oesopageal candidiasis
In non HIV patient: Invasive Aspergillosis, systemic candidiasis
- Gram negative infection (Pseudomonas Aeruginosa, Alcalagines sp)

« Nouveaux outils »: beta D Glucan

- Seuil (double seuil)
- VPN>>> pour Dg de PCP
- VPP>>> pour différencier colo/Dg
- **Non SP >> autres IFI**
- **Faux positifs**
- Faux négatifs
- Pas de test unitaire
- Délai pour Dg

Other medical condition
Mucositis, neutropenia (excluding Gram negative infection and IFI)

Therapeutic
Albumin perfusion
Immunoglobulin
Antibiotics
Haemodialysis
use of cellulose membrane in extracorporeal epuration, certains gauzes on mucosal or serosal surface
administration of blood products produced through cellulose filters

« Nouveaux outils »: beta D Glucan

- Seuil (double seuil)
- Non SP >> autres IFI
- VPN>>> pour Dg de PCP
- VPP>>> pour différencier colo/Dg
- Faux positifs
- **Faux négatifs**
- Pas de test unitaire
- Délai pour Dg

- PJP colonization
- Lipemic blood samples
- Hemolyzed blood samples
- Certain fungi that lack significant levels of (1-3)-β-D-glucan such as *Zygomycetes, Cryptococcus neoformans, and Blastomyces dermatitidis*.

« Nouveaux outils »: beta D Glucan

- Seuil (double seuil)
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- Faux positifs
- Faux négatifs
- **Pas de test unitaire**
- **Délai pour Dg**

Kit	Manufacturer	FDA approved	Crab species	Cut off value
Fungitell	Associates of Cape Cod (U.S.)	Yes	*Limulus polyphemus (colormetric)*	60–80 pg/mL
Endostafe-PTS glucan	Charles River Laboratories (U.S.)	No	*Limulus polyphemus (colormetric)*	10–1000 pg/mL
Fungitec G-MK	Seikagaku Biobusiness (Japan	No	*Tachypleus tridentalus (colormetric)*	20 pg/mL
β-glucan test	Waco Pure Chemical Industries (Japan)	No	*Tachypleus tridentalus (turbidimetric)*	11 pg/mL
BGSTAR β-glucan test	Maruha (Japan)	No	*Tachypleus tridentalus (colormetric)*	11 pg/mL

« Nouveaux outils »: Limites méthodologiques

- Gold standard moins bon que nouveaux outils >>> redéfinir les maladies (avis d'expert)
- Standardisation (qPCR) >> seuil
- FP des BDG >>> Réduction par identification cause non infectieuse de BDG+
- VPP/VPN >>> proba pré test = Fce de la maladie
    - >>> score clinique
    - >>> implication des cliniciens
- Etudes>>> rétrospectives+ cas-contrôle avec biais énorme sur contrôle
- Meta analyse >>> études de mauvaises qualité limitent la portée d'une méta analyse même bien faite
- Disponibilité/timing >>> test unitaire

ECIL guidelines for the diagnosis of *Pneumocystis jirovecii* pneumonia in patients with haematological malignancies and stem cell transplant recipients

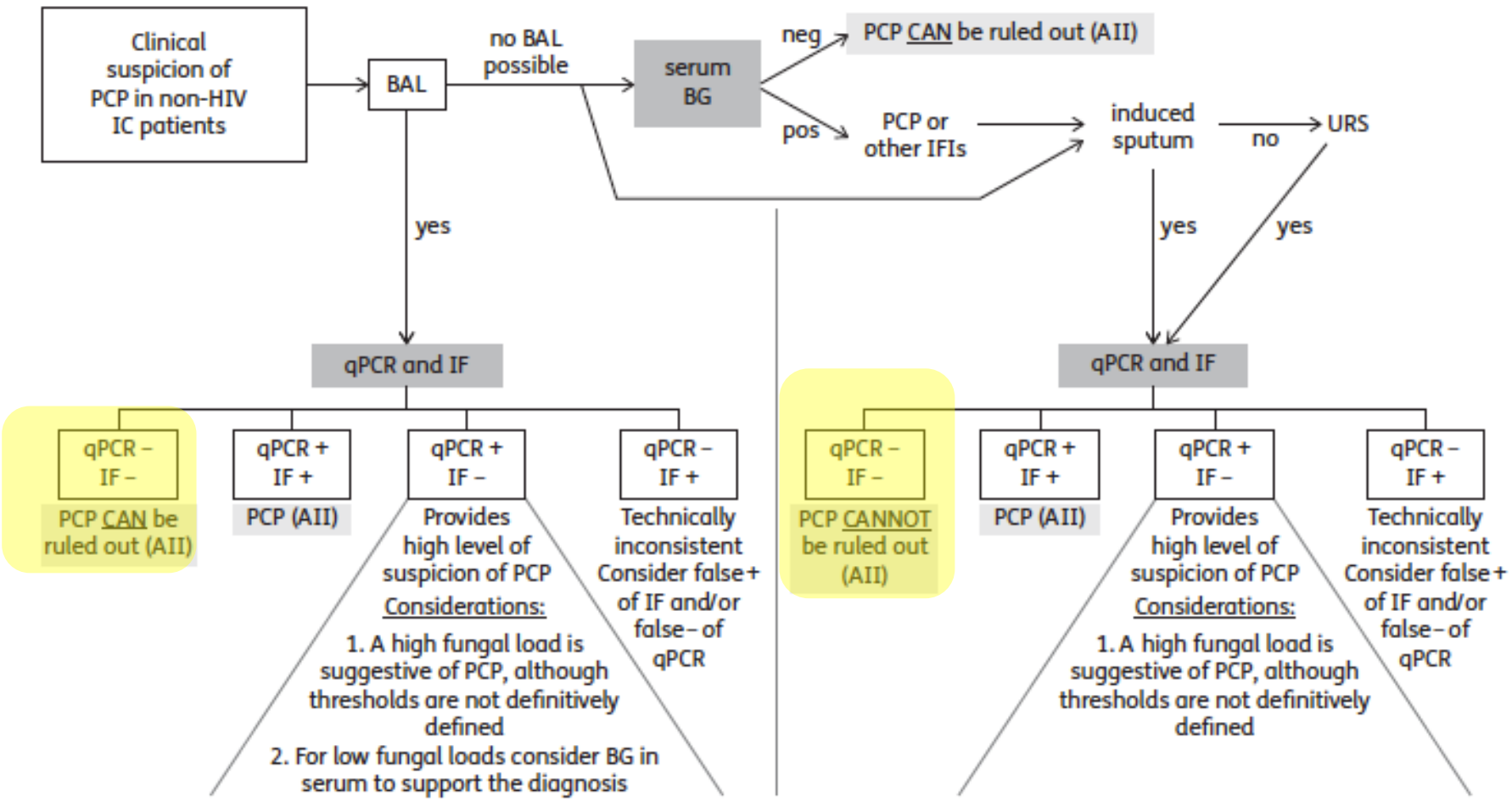

Figure 1. Flow chart for the diagnosis of *Pneumocystis* pneumonia in non-HIV immunocompromised (IC) patients. Biological tests are highlighted in dark grey and recommendations in light grey. BG, β-D-glucan; A-II, level of recommendation; IFI, invasive fungal infection.

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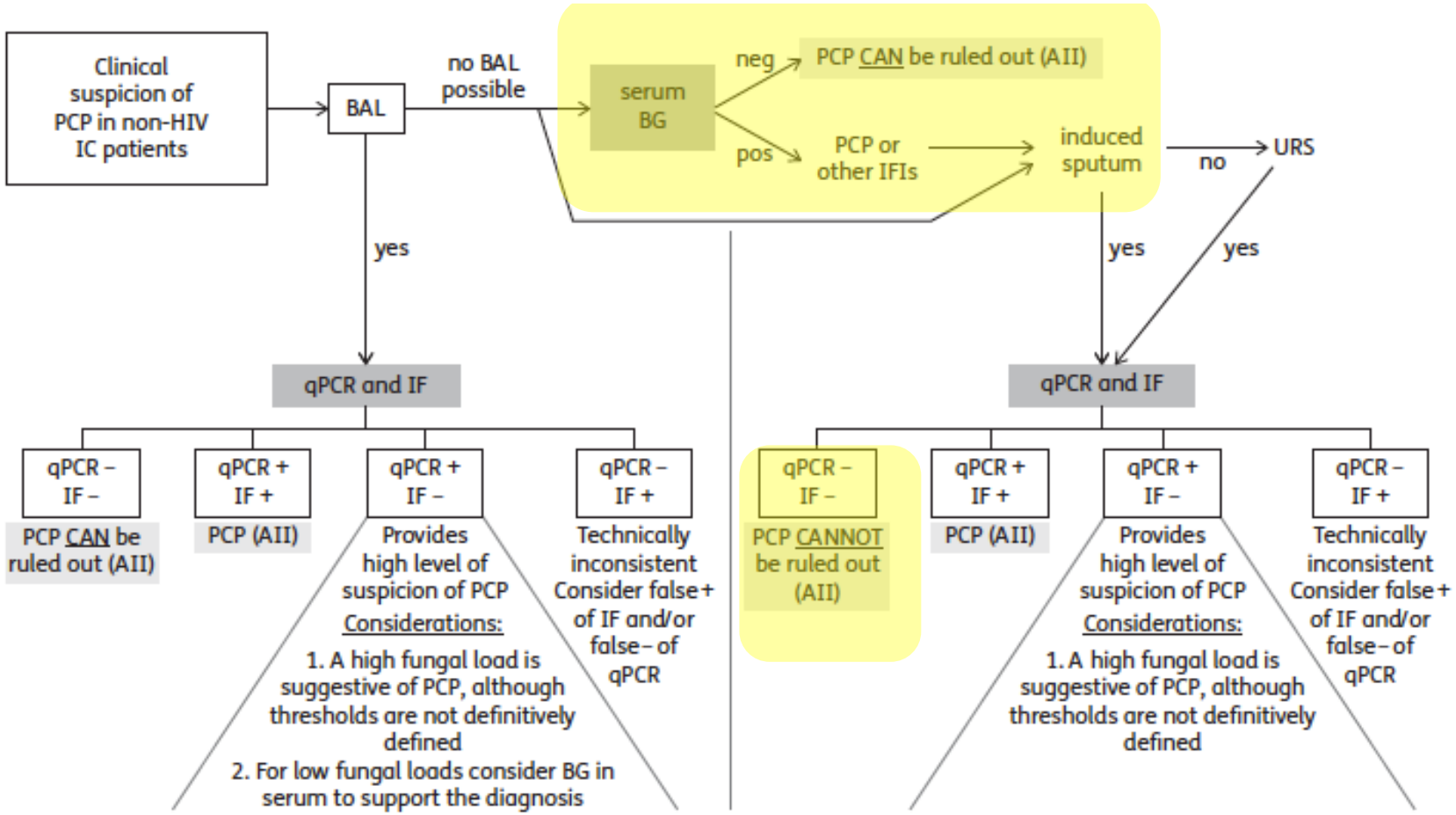


Figure 1. Flow chart for the diagnosis of *Pneumocystis* pneumonia in non-HIV immunocompromised (IC) patients. Biological tests are highlighted in dark grey and recommendations in light grey. BG, β-D-glucan; A-II, level of recommendation; IFI, invasive fungal infection.

Pneumocystis jirovecii Disease: Basis for the Revised EORTC/MSGERC Invasive Fungal Disease Definitions in Individuals Without Human Immunodeficiency Virus

Proven PCP	• Clinical and radiologic criteria, plus: - Demonstration of *P. jirovecii* by microscopy using conventional or immunofluorescence staining in tissue or - Demonstration of *P. jirovecii* by microscopy using conventional or immunofluorescence staining in respiratory specimens	Probable PCP	• Appropriate host factors and clinical and radiologic criteria, plus: - Amplification of *P. jirovecii* DNA by quantitative real-time PCR in respiratory specimen or - Detection of β-D-glucan in serum (alternative method; another IFD and a false-positive result should be ruled out)

Lagrou, CID, 2021

Pronostic

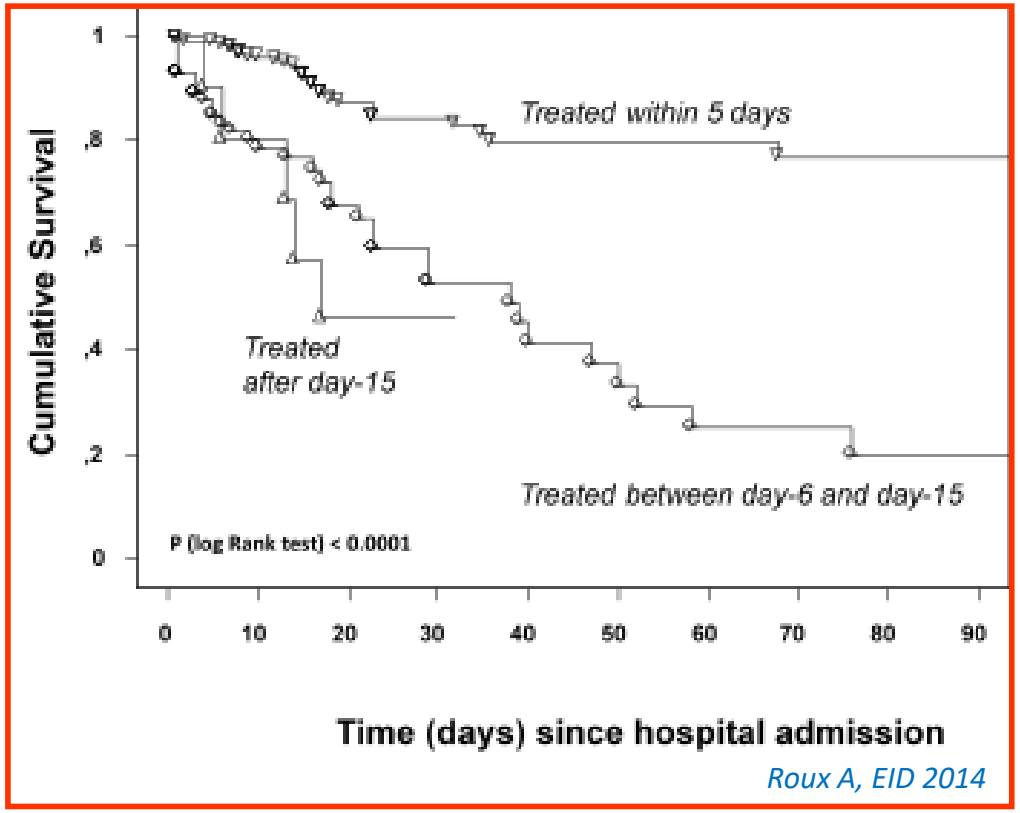
Gravité

- Admission en réa= 50%
- VM= 30%

- Mortalité
  - 4%-10% pour VIH
  - 20-40% non VIH
  - >80% si VM

Facteurs de risque de mortalité

Variable	Odds ratio
VIH+	OR 0.33, 95% CI [0.12-0.92]
Transplantation d'organe	OR 0.08, 95% CI [0.02-0.31]
Age	OR 1.04/a, 95% CI [1.02-1.06]
Allogreffe de CSH	OR 8.6, 95% CI [1.40-53.02]
Besoin d'O2 dès l'admission	OR 4.06, 95% CI [1.44-11.5]
Besoin de VM	OR 16.70, 95% CI [7.25-38]
Délai de traitement	OR 1.11/j, 95% CI [1.04-1.18]



Roux A, EID 2014

Traitement curatif

- INITIATION du traitement dès la suspicion SANS attendre les prlvts ni les résultats
- ≥14jrs

Table 2. Treatment of Pneumocystis Pneumonia.

Drug	Dose	Route	Comments
Trimethoprim–sulfamethoxazole	15–20 mg/kg 75–100 mg/kg daily in divided doses	Oral or intravenous	First choice
Primaquine plus clindamycin	30 mg daily 600 mg three times daily	Oral	Alternate choice
Atovaquone	750 mg two times daily	Oral	Alternate choice
Pentamidine	4 mg/kg daily 600 mg daily	Intravenous Aerosol	Alternate choice

Thomas, NEJM 2004
ECIL, 2016

Traitement curatif- Corticothérapie adjuvante.

Contexte HIV
• ECR • Bozette, NEJM, 1990, n=333 (PaO2>75)) • Gagnon, NEJM, 1990, n=23 (PaO2<75) • Diminution insuffisance respiratoire +mortalité

Contexte non HIV		
• Etudes rétrospectives • Résultats contradictoires		
↘mortalité *Pareja, 1998* *Inoue, 2019*	**Ø effet** *Delclaux, CID, 1999* *Moon, 2011*	**↑mortalité** *Lemiale, 2013*

Protocoles proposés

- **Bozette: Prednisone**
  40mg x2/J 5jrs
  puis 40mg/J pdt 5jrs
  puis 20mg pdt 5jrs
- **Gagnon (72hrs du tt ATB)**
  Methylprednisone 40mg x4/J, 7jrs
- **Pareja: Prednisone**
  ≥ 60mg/J
- **Moon, Prednisone**
  40mg x2/J pdt 5jrs
- **PHRC: Methylprednisone**

Day 1 to 5 : 30mg twice per day
Day 6 to 10 : 30mg per day
Day 11 to 21 : 20mg per day

Traitement préventif

HIV: CD4<200

Non HIV: cf Terrain

- *PCP que chez des patients sans prophylaxie avec mortalité 30-50%*
- Si prophylaxie avait été interrompue reprendre après intensification IS

Table 1. Drugs for Prophylaxis against Pneumocystis Pneumonia.

Drug	Dose	Route	Comments
Trimethoprim–sulfamethoxazole	1 double-strength tablet daily or 1 single-strength tablet daily	Oral	First choice
	1 double-strength tablet 3 times per week		Alternate choice
Dapsone	50 mg twice daily or 100 mg daily	Oral	Ensure patient does not have glucose-6-phosphate dehydrogenase deficiency
Dapsone plus pyrimethamine plus leucovorin	50 mg daily 50 mg weekly 25 mg weekly	Oral	
Dapsone plus pyrimethamine plus leucovorin	200 mg weekly 75 mg weekly 25 mg weekly	Oral	
Pentamidine	300 mg monthly	Aerosol	
Atovaquone	1500 mg daily	Oral	Give with high-fat meals, for maximal absorption

Messages

- Terrain
- Absence de prophylaxie
- Verre dépoli= PCP jusqu’à preuve du contraire

Questions non résolues

- Place des BDG? de la qPCR/approche non invasive?
- Chez qui arrêter la prophylaxie?
- Cas groupés; isolement?
- Colonisation vs. Maladie?
- Corticothérapie adjuvante?
- Hétérogénéité des patients non VIH?

Merci de votre attention

@drAntoineRoux

L'étude qui n'existe pas

1st run by physician not biologist

4200 suspicion of PCP

2021-2022
non HIV patients
Multicentric
Prospective

Pre Test probality

Azoulay score

Underlying disease
Prophylaxis
CTscan aspect

	Low PCP pretest probability			**High PCP pretest probability**		
	noPCP	PCPcolo	PCPdisease	noPCP	PCPcolo	PCPdisease
BDG	- *NPV*	-	+	-	-	+ *PPV*
qPCR	- *NPV*	+ *Threshold*	+	-	+ *Threshold*	+
Colo	-	-	+	-	-	+
IF	-	-	+	-	-	+

You both,NEJM, 2023