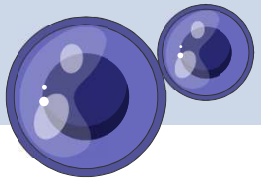
Infections fongiques chez la PVVIH



Actualités en infectiologie - 2025

Dr Anne Coste – CHU de Brest, France

WHO fungal priority pathogens

HIV and fungal priority pathogens

Hatim Sati, Ana Alastruey-Izquierdo, John Perfect, Nelesh P Govender, Tom S Harrison, Tom Chiller, Tania C Sorrell, Felix Bongomin, Rita Oladele, Arunaloke Chakrabarti, Retno Wahyuningsih, Arnaldo Lopes Colombo, Juan Luis Rodriguez-Tudela, Chris Beyrer, Nathan Ford

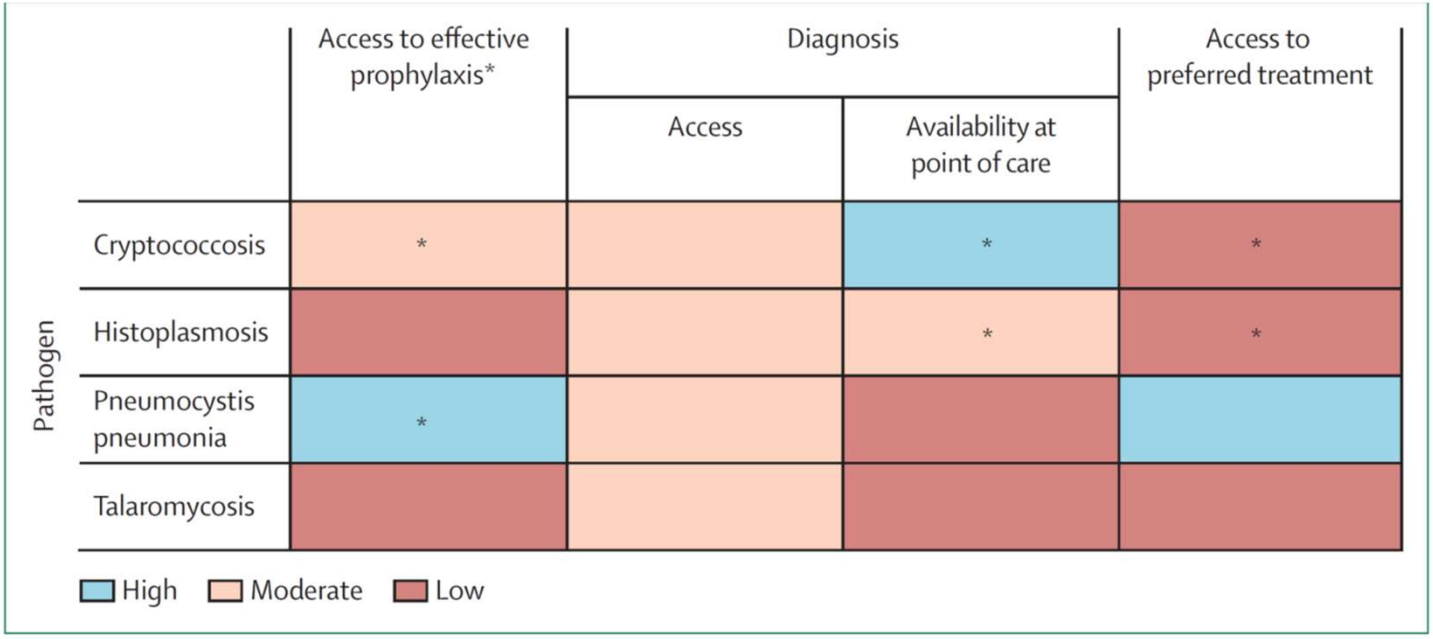


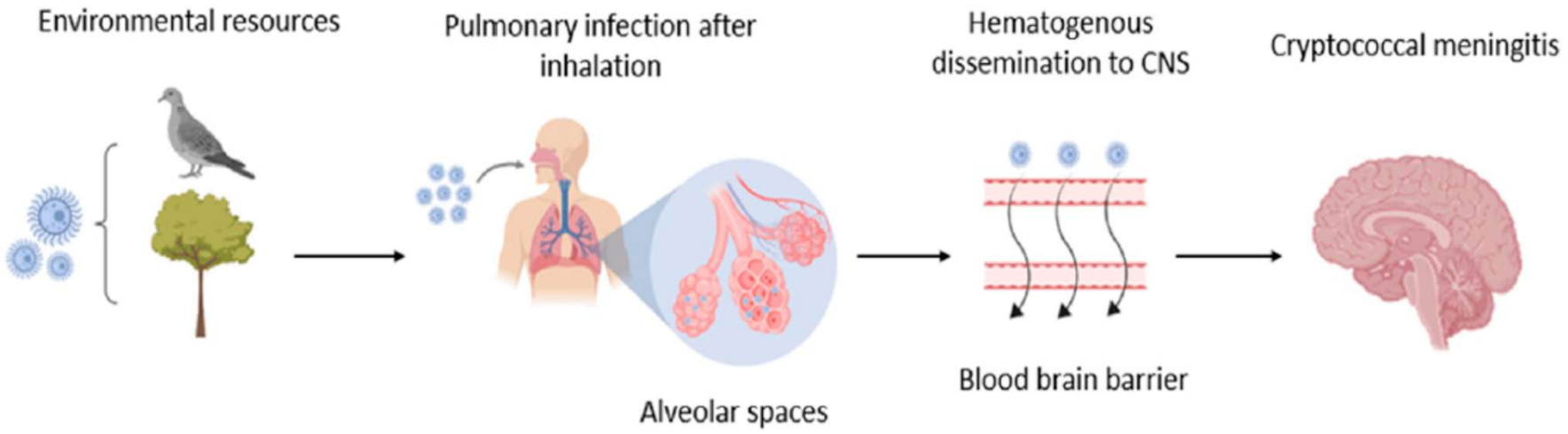
Figure: **Prevention, diagnosis, and treatment of HIV-associated infections caused by priority fungal pathogens in low-income and middle-income countries**

*Intervention recommended by WHO guidelines.

Sati *et al.*, Lancet HIV 2023

Cryptococcose chez PVVIH

- *Cryptococcus neoformans* : levure encapsulée
- Cryptococcose neuroméningée : clinique souvent frustre (céphalées, fièvre, raideur de nuque)
- Formes disséminées fréquentes chez la PVVIH : atteinte pulmonaire, hémoculture



Roosen *et al.*, J. Fungi 2024

Impact de la cryptococcose chez les PVVIH

- En Afrique subsaharienne :
- 4,4-6% des PVVIH avec <200 CD4+ ont un Ag cryptocoque positif
- Environ 71 000 décès/an
- 19% des décès liés au VIH : stable par rapport à 2014

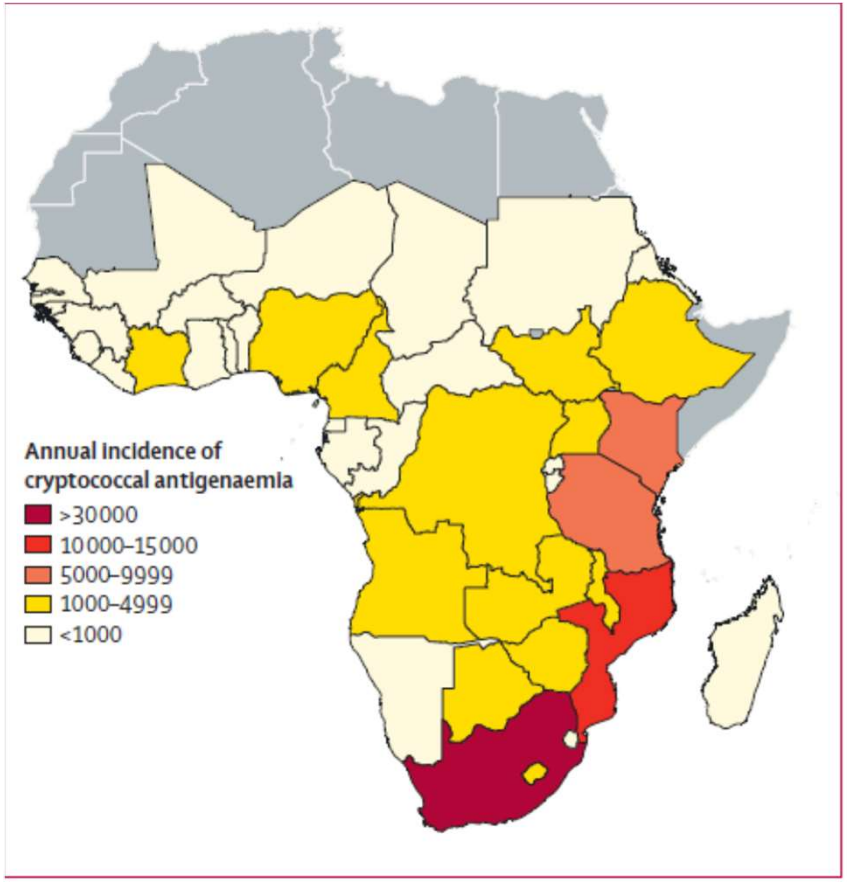
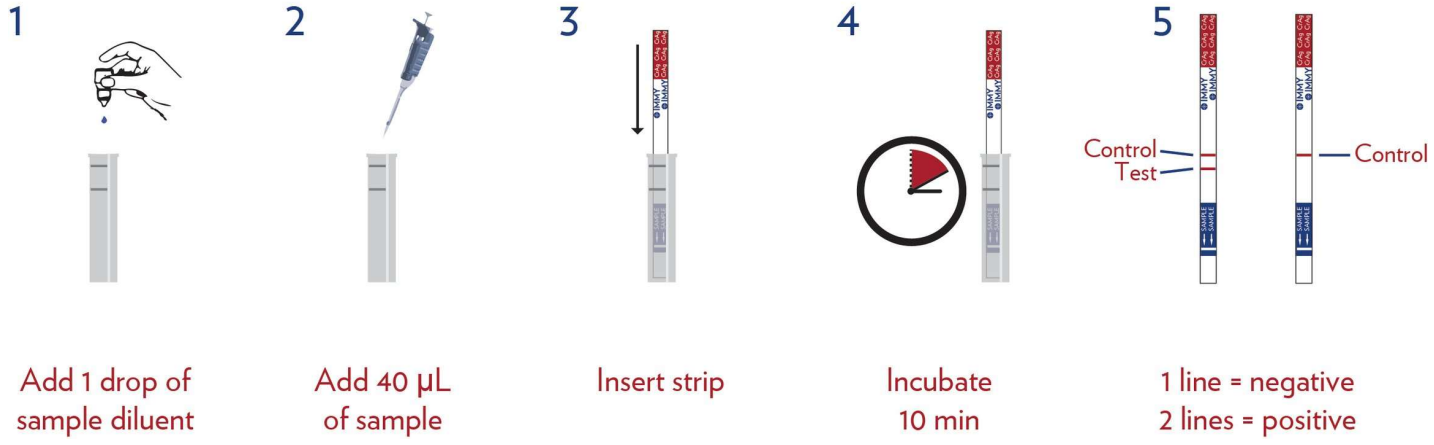


Figure 4: Annual incidence of cryptococcal antigenemia in sub-Saharan Africa

Rajasingham *et al.*, Lancet Infect Dis 2022

Diagnostic de la cryptococcose

- Examen direct : encre de Chine (LCR)
- Culture (LCR, sang, urines, expectoration)
- Lateral Flow Assay : AgCr (LCR, sang)

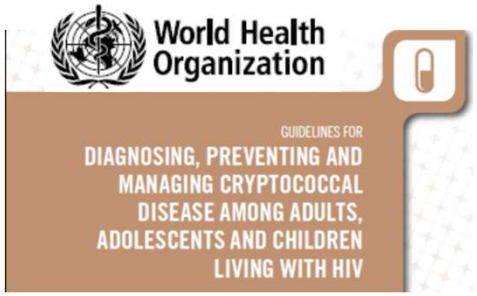


Diagnostic

- Si la PL n'est pas possible, un AgCr + dans le sang en présence de symptôme suffit à retenir le diagnostic

Summary of the diagnostic approach to cryptococcal meningitis

	Lumbar puncture available	Lumbar puncture not available or contraindicated
Rapid cryptococcal antigen test available	CSF cryptococcal antigen (preferably lateral flow assay)	Serum, plasma or whole-blood cryptococcal antigen (preferably lateral flow assay), treat immediately and refer for further investigation
No rapid cryptococcal antigen test available	CSF India ink	Prompt referral for further investigation



- Bilan d'extension (cas suspects ou confirmés, y compris antigénémie Cr) : rechercher extensivement une cryptococcose disséminée
  - PL, Ag+culture sang, Ag+culture expectorations, IRM cérébrale et TDM thoracique
  - Attention si AgCr sang + : confirmer une encre de Chine négative sur LCR par un AgCr (meilleure sensibilité)

WHO 2022

Diagnostic de la CN

Clinical Infectious Diseases
REVIEW ARTICLE

Cryptococcal Antigen in Serum and Cerebrospinal Fluid for Detecting Cryptococcal Meningitis in Adults Living With Human Immunodeficiency Virus: Systematic Review and Meta-Analysis of Diagnostic Test Accuracy Studies

Elvis Temfack,[1,2,©] Jean Joel Bigna Rim,[3] Rene Spijker,[4] Angela Loyse,[5,6,7] Tom Chiller,[8] Peter G. Pappas,[9] John Perfect,[10] Tania C. Sorell,[11] Thomas S. Harrison,[5,6,7] Jérémie F. Cohen,[12,13] and Olivier Lortholary[1,14]

- 11 études inclues, 3600 participants VIH+ avec symptômes neurologiques
- Diagnostic de cryptococcose neuroméningée retenue chez 43% des patients
- Reference : culture+ ou encre de Chine+ sur le LCR)

Table 3. Summary of Diagnostic Accuracy Findings

		Quantity of evidence		Summary estimates	
Sample	Test type	Cohorts, n	Participants, n	Sensitivity, % (95% CI)	Specificity, % (95% CI)
Serum	LA	5	256	100 (99.5–100)[a]	96.7 (93.8–98.9)[a]
	LFA	3	1690	97.9 (87.9–100)[a]	89.5 (74.3–98.5)[a]
	Overall serum CrAg	8	1946	99.7 (97.4–100)[b]	94.1 (88.3–98.1)[b]
	P value[c]	8	-	.08	.16
CSF	LA	10	1810	97.1 (91.9–99.0)[b]	99.1 (93.8–99.9)[b]
	LFA	6	3099	99.5 (97.2–99.9)[b]	99.5 (94.2–100)[b]
	Overall CSF CrAg	16	3500	98.8 (96.2–99.6)[b]	99.3 (96.7–99.9)[b]
	P value[c]	16	-	.07	.54

Temfack *et al.*, Clin Infect Dis 2021

Screening par AgCr sang

- Au diagnostic ou à la reprise des ARV :
  - chez toute personne ayant < 100 CD4/mm^3 (WHO guidelines),
  - chez toute personne ayant < 200 CD4/mm^3 (ECMM & ISHAM guidelines)
- Si screening impossible (ou délai de rendu long) en zone de forte endémie :
  - traitement pré-emptif par Fluconazole chez les PVVIH avec CD4<100/mm^3 (<200/mm^3 selon ECMM & ISHAM guidelines)

Panel 4: Recommendations for screening, primary prophylaxis, and pre-emptive therapy

Adults living with HIV who are antiretroviral therapy (ART)-naive or after a period of ART discontinuation with less than 200 CD4 cells per mm^3 must have:

- (AI) A lateral flow assay of blood cryptococcal antigen for the screening of cryptococcosis and the cryptococcal antigen titre should be measured if positive
- (AIIt) All patients with cryptococcal antigenaemia should be carefully assessed and investigated for cryptococcosis and treated as appropriate

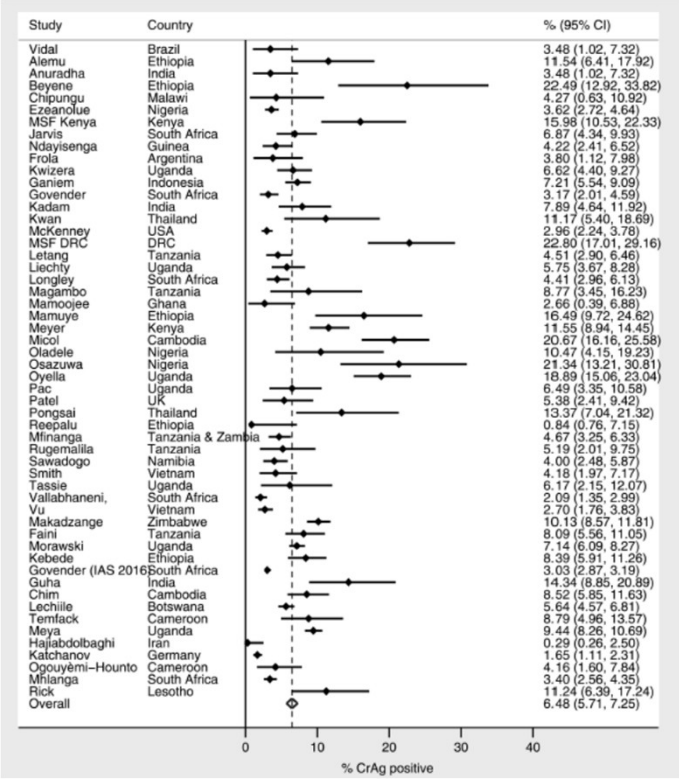
Global guideline for the diagnosis and management of cryptococcosis: an initiative of the ECMM and ISHAM in cooperation with the ASM

Christina C Chang, Thomas S Harrison, Tihana A Bicanic, Methee Chayakulkeeree, Tania C Sorrell, Adilia Warris, Ferry Hagen, Andrej Spec, Rita Oladele, Nelesh P Govender, Sharon C Chen, Christopher H Mody, Andreas H Groll, Yee-Chun Chen, Michail S Lionakis, Alexandre Alanio, Elizabeth Castañeda, Jairo Lizarazo, José E Vidal, Takahiro Takazono, Martin Hoenigl, Jan-Willem Alffenaar, Jean-Pierre Gangneux, Rajeev Soman, Li-Ping Zhu, Alexandro Bonifaz, Joseph N Jarvis, Jeremy N Day, Nikolai Klimko, Jon Salmanton-García, Grégory Jouvion, David B Meya, David Lawrence, Sebastian Rahn, Felix Bongomin, Brendan J McMullan, Rosanne Sprute, Tinashe K Nyazika, Justin Beardsley, Fabianne Carlesse, Christopher H Heath, Olusola O Ayanlowo, Olga M Mashedi, Flavio Queiroz-Telles Filho, Mina C Hosseinipour, Atul K Patel, Elvis Temfack, Nina Singh, Oliver A Cornely, David R Boulware, Olivier Lortholary, Peter G Pappas, John R Perfect

Chang *et al.*, Lancet Infect Dis 2024

Screening : taux CD4

- Prévalence d'AgCr+ selon le taux de CD4
- 60 études inclues, variabilité importante

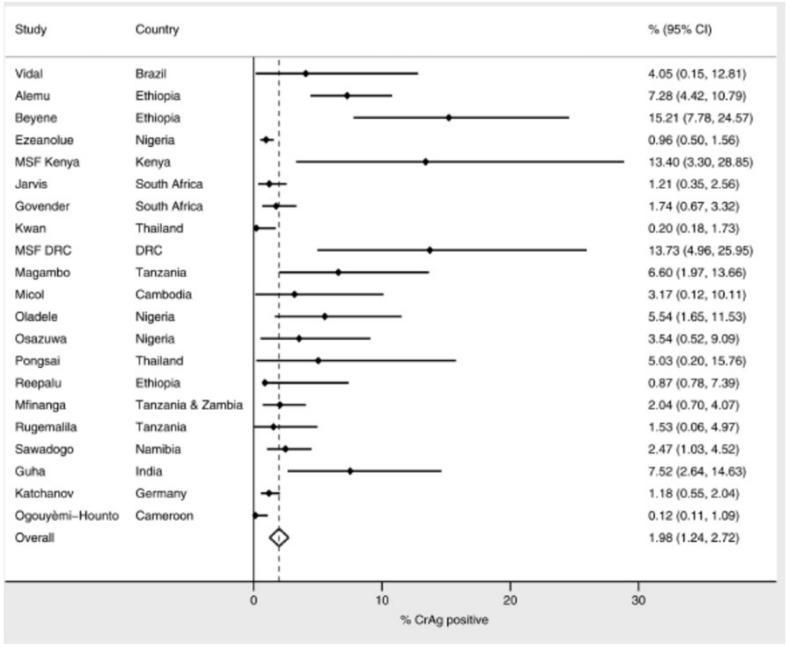


Si CD4<100/mm^3 : 6,5%

Clinical Infectious Diseases
SUPPLEMENT ARTICLE

CD4 Cell Count Threshold for Cryptococcal Antigen Screening of HIV-Infected Individuals: A Systematic Review and Meta-analysis

Nathan Ford,[1] Zara Shubber,[2] Joseph N. Jarvis,[3,4,5] Tom Chiller,[6] Greg Greene,[5] Chantal Migone,[1] Marco Vitoria,[1] Meg Doherty,[1] and Graeme Meintjes[7,8]



Si CD4<200/mm^3 : 2%

Ford *et al.*, Clin Infect Dis 2018

Screening : impact

- Evaluation de l'impact du screening pré-hospitalier sur la mortalité à J14 en Ouganda
- 489 patients <100 CD4 inclus (194 avec screening préalable) dont 47% sous ARV
- Période 2018-2021
- Impact significatif en univarié mais pas en multivarié

Clinical Infectious Diseases
MAJOR ARTICLE

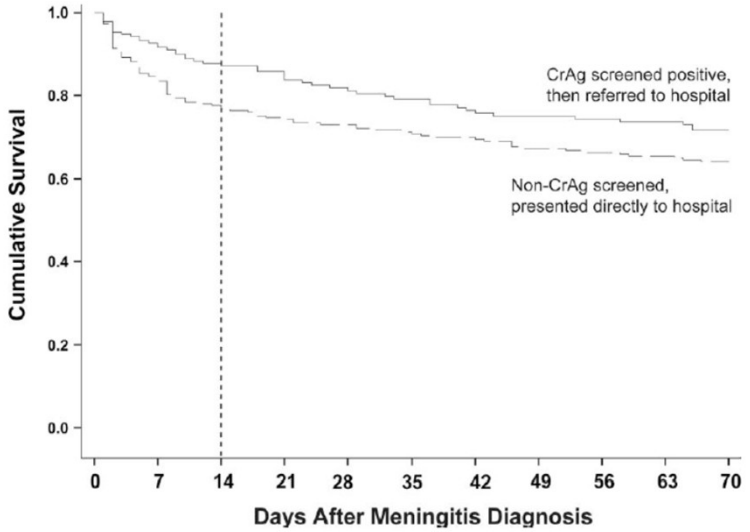
Outpatient Cryptococcal Antigen Screening Is Associated With Favorable Baseline Characteristics and Improved Survival in Persons With Cryptococcal Meningitis in Uganda

Anna E. Levin,[1] Ananta S. Bangdiwala,[2] Elizabeth Nalintya,[3] Enock Kagimu,[3] John Kasibante,[3] Morris K. Rutakingirwa,[3] Edward Mpoza,[3] Samuel Jjunju,[4] Edwin Nuwagira,[4] Rose Naluyima,[3] Paul Kirumira,[3] Cody Hou,[1,©] Kenneth Ssebambulidde,[3] Abdu K. Musubire,[3] Darlisha A. Williams,[1] Mahsa Abassi,[1,©] Conrad Muzoora,[4] Katherine H. Hullsiek,[2] Radha Rajasingham,[1,©] David B. Meya,[1,3,5,a] David R. Boulware,[1,a] and Caleb P. Skipper[1,3,a,©]

Table 2. Proportional Hazards Model for 14-Day Mortality of Participants With Cryptococcal Meningitis By CrAg Screening Status

	Univariate			Multivariate		
Variable	Hazard Ratio	95% CI	*P*	Hazard Ratio	95% CI	*P*
CrAg screened	.51	.32–.83	.006	.63	.37–1.08	.09
Glasgow Coma Scale score <15	4.87	3.05–7.76	<.001	5.22	3.03–8.98	<.001
CSF WBC count <5 cells/μL	1.83	1.13–2.96	.01	2.15	1.23–3.77	.007
CSF culture, per $\log_{10}$ CFU/mL	1.18	1.05–1.33	<.001	1.11	.98–1.26	.11
CSF opening pressure >250 mmH_2O	1.60	1.05–2.45	.03	1.25	.76–2.05	.38
Baseline seizure	1.82	1.24–2.67	.002	1.13	.70–1.84	.61
Receiving ART at baseline	.93	.60–1.43	.73	1.53	.94–2.49	.09
Randomized to AmBisome[a]	1.00	.64–1.56	.99	1.23	.75–2.01	.42
Age, per year	1.01	.99–1.03	.36	1.01	.99–1.03	.40
Male	.89	.58–1.37	.60	.71	.43–1.16	.17

A multivariate proportional hazards model for 14-day mortality was used to adjust for contributing meningitis risk factors. CrAg screening was no longer significantly associated with mortality after multivariate adjustment, while Glasgow Coma Scale score <15 and CSF WBC count <5 cells/μL remained significantly associated.
Abbreviations: ART, antiretroviral therapy; CFU, colony forming units; CI, confidence interval; CrAg, cryptococcal antigen; CSF, cerebrospinal fluid; WBC, white blood cell.
[a]liposomal amphotericin B 10mg/kg by Gilead Sciences, Inc.



Levis *et al.*, Clin Infect Dis 2023

Screening : impact

- Evaluation de l'impact du screening pré-hospitalier la mortalité intra hospitalière en Afrique du Sud
- 3390 patients <100 CD4 inclus (830 avec screening préalable) sur 2017-2021
- Résultats :
  - Moins de troubles de conscience chez les patients screenés (38% vs 43%)
  - Impact significatif en univarié mais pas en multivarié
  - SAUF durant la période COVID → difficultés d'accès aux soins ?

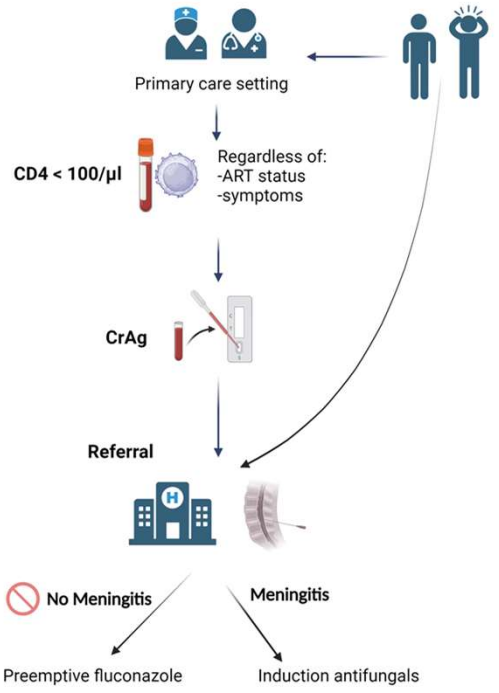
Le screening permet de détecter des cas non symptomatiques
La détection avant l'apparition des troubles neurologiques est associée à un meilleur pronostic

Contents lists available at ScienceDirect
Clinical Microbiology and Infection
journal homepage: www.clinicalmicrobiologyandinfection.com

Original article

Impact of prior cryptococcal antigen screening on in-hospital mortality in cryptococcal meningitis or fungaemia among HIV-seropositive individuals in South Africa: a cross-sectional observational study

Olivier Paccoud [1,2], Liliwe Shuping [1], Rudzani Mashau [1], Greg Greene [1], Vanessa Quan [3], Susan Meiring [3,4], Nelesh P. Govender [1,5,6,7,8,*], for GERMS-SA[†]



Paccoud *et al.*, Clin Microbiol Infect 2023

Traitement

Global guideline for the diagnosis and management of cryptococcosis: an initiative of the ECMM and ISHAM in cooperation with the ASM

Christina C Chang, Thomas S Harrison, Tihana A Bicanic, Methee Chayakulkeeree, Tania C Sorrell, Adilia Warris, Ferry Hagen, Andrej Spec, Rita Oladele, Nelesh P Govender, Sharon C Chen, Christopher H Mody, Andreas H Groll, Yee-Chun Chen, Michail S Lionakis, Alexandre Alanio, Elizabeth Castañeda, Jairo Lizarazo, José E Vidal, Takahiro Takazono, Martin Hoenigl, Jan-Willem Alffenaar, Jean-Pierre Gangneux, Rajeev Soman, Li-Ping Zhu, Alexandro Bonifaz, Joseph N Jarvis, Jeremy N Day, Nikolai Klimko, Jon Salmanton-García, Grégory Jouvion, David B Meya, David Lawrence, Sebastian Rahn, Felix Bongomin, Brendan J McMullan, Rosanne Sprute, Tinashe K Nyazika, Justin Beardsley, Fabianne Carlesse, Christopher H Heath, Olusola O Ayanlowo, Olga M Mashedi, Flavio Queiroz-Telles Filho, Mina C Hosseinipour, Atul K Patel, Elvis Temfack, Nina Singh, Oliver A Cornely, David R Boulware, Olivier Lortholary, Peter G Pappas, John R Perfect

- Cryptococcose neuroméningée, disséminée ou pulmonaire sévère (ECMM & ISHAM):

First-line therapies

Induction (2 weeks)
(AIIt) Liposomal amphotericin B 3–4 mg/kg daily plus flucytosine 25 mg/kg four times a day (preferred in high-income settings); or
(AI) Single dose liposomal amphotericin B 10 mg/kg and 14 days of flucytosine 25 mg/kg four times a day and fluconazole 1200 mg daily (recommended in low-income settings)

→

Consolidation (8 weeks)
(AI) Fluconazole 400–800 mg daily (800 mg preferred in low-income settings)

→

Maintenance (12 months or until immune restoration)
(AIIt) Fluconazole 200 mg daily

- WHO guidelines 2022 :
  - Induction : schéma single dose L-AmB uniquement
  - Consolidation : fluconazole 800mg/j

- Recommandations françaises 2024 :
  - Induction : schéma L-AmB 7j + 5-FC positionnée
  - Consolidation 800mg/j

World Health Organization

GUIDELINES FOR
DIAGNOSING, PREVENTING AND MANAGING CRYPTOCOCCAL DISEASE AMONG ADULTS, ADOLESCENTS AND CHILDREN LIVING WITH HIV

Chang *et al.*, Lancet Infect Dis 2024
WHO 2022
HAS 2024

Induction

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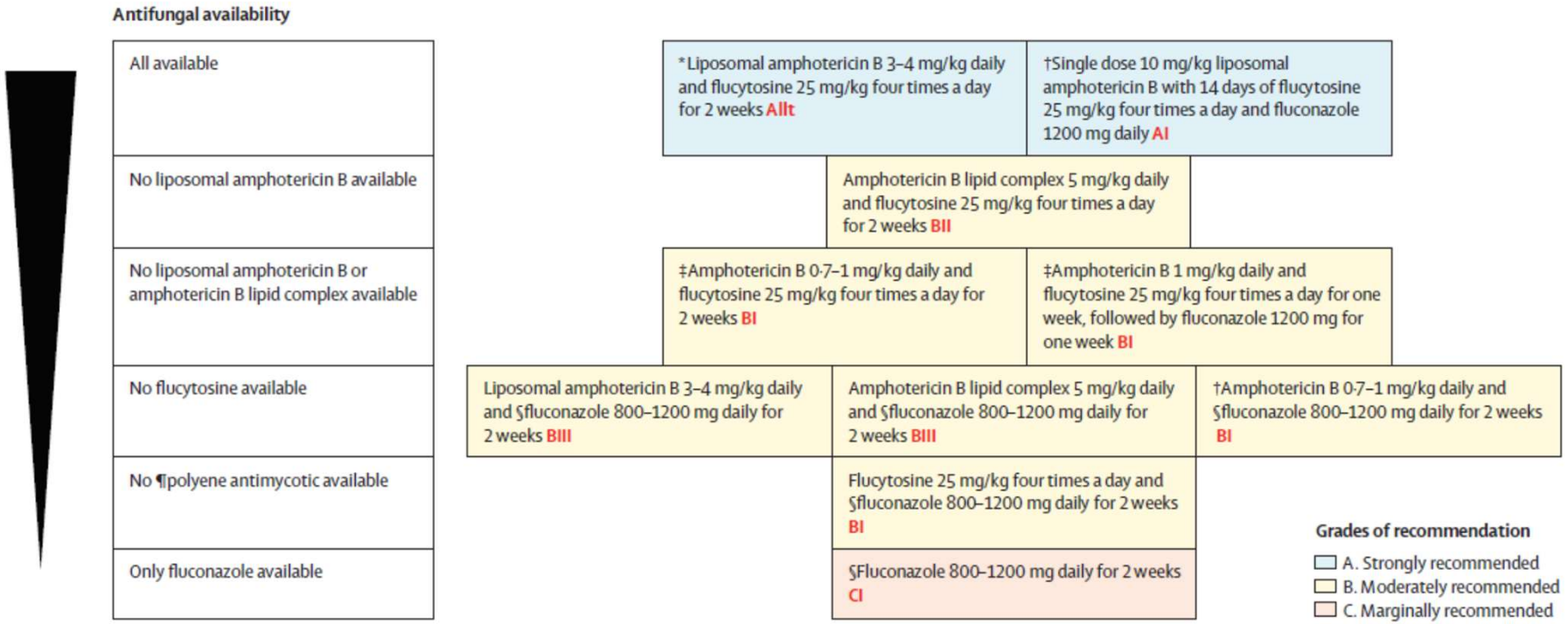


Chang *et al.*, Lancet Infect Dis 2024

Traitement

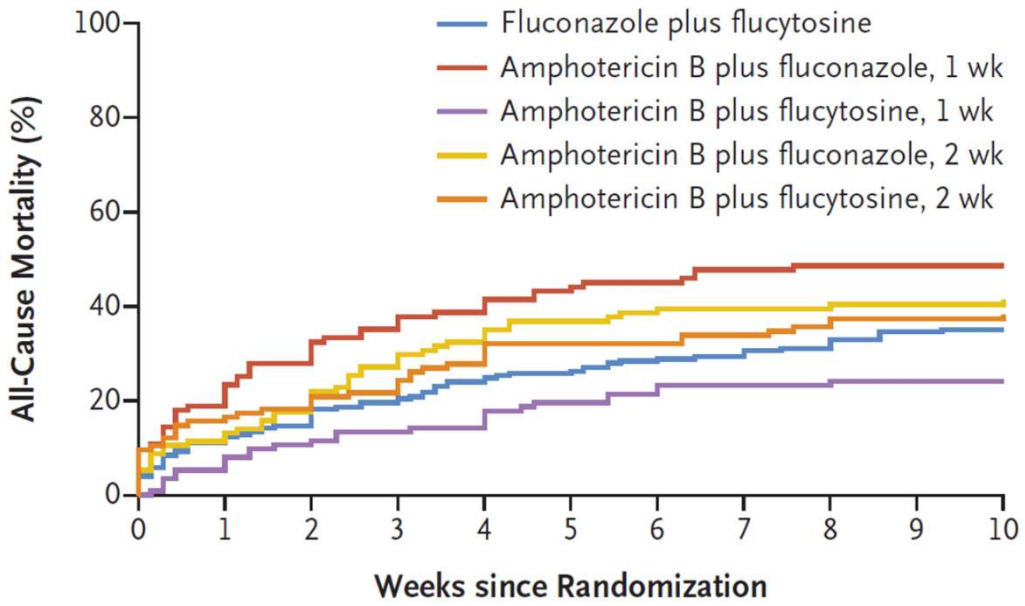
- Essai randomisé contrôlé, 721 patients (Malawi, Zambie, Tanzanie, Cameroun)
  - 3 bras (FCZ+5FC, AmB désoxycholate 1s, AmB 2s)
  - Chaque gpe AmB divisé en AmB+FCZ et AmB+5FC
  - Troubles de conscience ~45%, ARV ~55%
- Résultats survie à 10s:
  - Groupe avec la meilleure survie : AmB 1s+5FC (76%)
  - Comparaison avec gpe « oral » (65%) : HR=1,56 (1.01-2.42)
  - Comparaison avec gpe AmB 2s+5-FC (59%): HR=1.97 (1.22-3.17)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

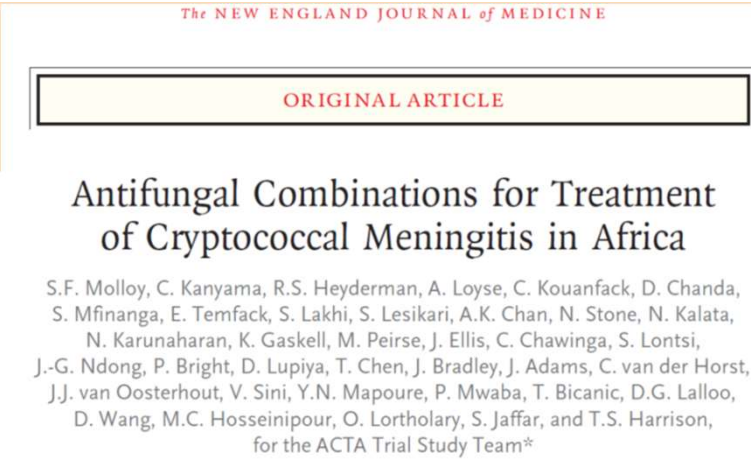
Antifungal Combinations for Treatment of Cryptococcal Meningitis in Africa

S.F. Molloy, C. Kanyama, R.S. Heyderman, A. Loyse, C. Kouanfack, D. Chanda, S. Mfinanga, E. Temfack, S. Lakhi, S. Lesikari, A.K. Chan, N. Stone, N. Kalata, N. Karunaharan, K. Gaskell, M. Peirse, J. Ellis, C. Chawinga, S. Lontsi, J.-G. Ndong, P. Bright, D. Lupiya, T. Chen, J. Bradley, J. Adams, C. van der Horst, J.J. van Oosterhout, V. Sini, Y.N. Mapoure, P. Mwaba, T. Bicanic, D.G. Lalloo, D. Wang, M.C. Hosseinipour, O. Lortholary, S. Jaffar, and T.S. Harrison, for the ACTA Trial Study Team*



Molloy *et al.*, NEJM 2018

Traitement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- Résultats : clairance du LCR
  - Supériorité du groupe AmB+5FC
- Effets indésirables biologiques plus fréquent dans le groupe AmB
  - Nécessité d'une transfusion : 5.5% (oral), 10.3% (AmB 1s) et 20.2% (AmB 2s)

→ L'administration d'amphotéricine B nécessite :
- un suivi biologique régulier
- des perfusions intraveineuses d'électrolytes
- une hospitalisation durant toute la durée du traitement

AMBITION

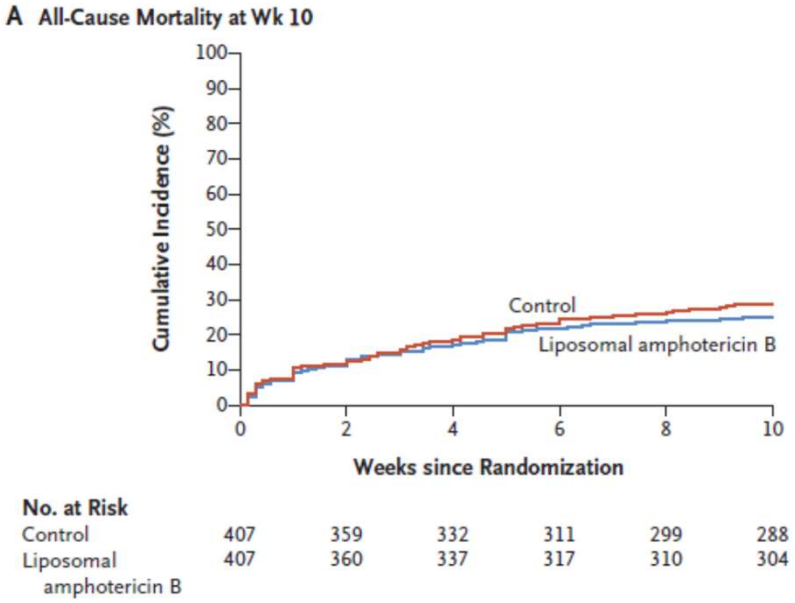
AMBITION-*cm*
AMBIsome Therapy Induction OptimizatioN

The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 MARCH 24, 2022 VOL. 386 NO. 12

Single-Dose Liposomal Amphotericin B Treatment for Cryptococcal Meningitis

J.N. Jarvis, D.S. Lawrence, D.B. Meya, E. Kagimu, J. Kasibante, E. Mpoza, M.K. Rutakingirwa, K. Ssebambulidde, L. Tugume, J. Rhein, D.R. Boulware, H.C. Mwandumba, M. Moyo, H. Mzinganjira, C. Kanyama, M.C. Hosseinipour, C. Chawinga, G. Meintjes, C. Schutz, K. Comins, A. Singh, C. Muzoora, S. Jjunju, E. Nuwagira, M. Mosepele, T. Leeme, K. Siamisang, C.E. Ndhlovu, A. Hlupeni, C. Mutata, E. van Widenfelt, T. Chen, D. Wang, W. Hope, T. Boyer-Chammard, A. Loyse, S.F. Molloy, N. Youssouf, O. Lortholary, D.G. Lalloo, S. Jaffar, and T.S. Harrison, for the Ambition Study Group*

- Essai de non-infériorité, 844 patients
- 1 bras AmB désoxycholate 1mg/kg/j + 5FC pdt 7 jours puis FCZ 1200mg/j pdt 7 jours
- 1 bras L-AmB 10mg/kg 1 dose unique associé à 5FC + FCZ pendant 14 jours



Ouganda, Malawi, Zimbabwe, Botswana, Afrique du Sud

Jarvis *et al.*, NEJM 2023

AMBITION

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Table 3. Laboratory-Defined and Clinical Adverse Events Occurring within 21 Days after Randomization.*

Event	Liposomal Amphtericin B (N=420)	Control (N=422)	P Value†
Grade 3 or 4 adverse events — no. of events	382	579	
Any grade 3 or 4 adverse event — no. of participants (%)			
Grade 3 or 4	210 (50.0)	263 (62.3)	<0.001
Grade 3	173 (41.2)	225 (53.3)	<0.001
Grade 4	91 (21.7)	127 (30.1)	0.005
Anemia — no. of participants (%)‡			
Grade 3	44 (10.5)	108 (25.6)	<0.001
Grade 4	12 (2.9)	62 (14.7)	<0.001
Mean change in hemoglobin level from baseline to day 7 — g/dl§	−0.3±1.39	−1.9±1.8	<0.001
Receipt of blood transfusion — no. of participants (%)	32 (7.6)	76 (18.0)	<0.001
Neutropenia — no. of participants (%)¶			
Grade 3	27 (6.4)	21 (5.0)	0.36
Grade 4	20 (4.8)	16 (3.8)	0.49
Thrombocytopenia — no. of participants (%)‖			
Grade 3	9 (2.1)	17 (4.0)	0.11
Grade 4	4 (1.0)	6 (1.4)	0.75
Creatinine increase — no. of participants (%)**			
Grade 3	17 (4.0)	22 (5.2)	0.42
Grade 4	5 (1.2)	3 (0.7)	0.51
Mean relative increase in creatinine level from baseline to day 7 — %††	20.2±48.1	49.7±70.8	<0.001
Hypokalemia — no. of participants (%)‡‡			
Grade 3	6 (1.4)	27 (6.4)	<0.001
Grade 4	0	3 (0.7)	0.25
Elevated ALT — no. of participants (%)§§			
Grade 3	6 (1.4)	4 (0.9)	0.52
Grade 4	1 (0.2)	1 (0.2)	1.0
Thrombophlebitis requiring antibiotic therapy — no. of participants (%)	8 (1.9)	28 (6.6)	<0.001
Other grade 3 or 4 adverse event — no. of participants (%)¶¶	167 (39.8)	173 (41.0)	0.72

- Critères secondaires :
  - Clairance du LCR similaire
  - Moins d'effets indésirables grade 3-4 dans le groupe L-AmB (50% *vs* 62%, p<0,001)

Jarvis *et al.*, NEJM 2023

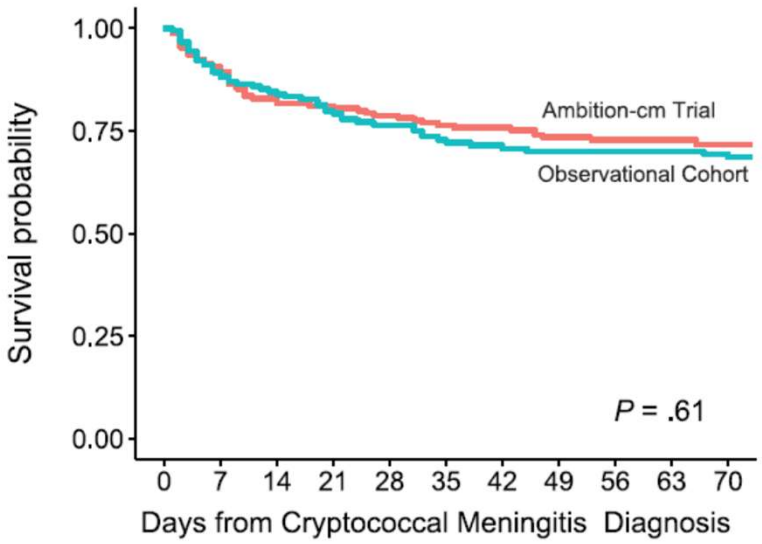
Traitement par L-AmB monodose

Clinical Infectious Diseases
MAJOR ARTICLE

Implementation of Single High-dose Liposomal Amphotericin B Based Induction Therapy for Treatment of HIV-associated Cryptococcal Meningitis in Uganda: A Comparative Prospective Cohort Study

Jane Gakuru,[1,6] Enock Kagimu,[1,6] Biyue Dai,[2] Samuel Okurut,[1] Laura Nsangi,[1] Nathan C. Bahr,[3] Michael Okirwoth,[1] Olivie C. Namuju,[1] Joseph N. Jarvis,[4,5] David S. Lawrence,[4,5,6] Cynthia Ahimbisibwe,[1] Jayne Ellis,[1,4] Kizza Kandole Tadeo,[1] David R. Boulware,[3,6] David B. Meya,[1,3,7,8] and Lillian Tugume[1]

- Quelle est l'efficacité du protocole AMBITION en vie réelle ?
  - 179 patients en Ouganda, comparé à 171 patients de l'essai AMBITION
  - Protocole L-AmB monodose + FCZ 1200mg/j + 5FC 100/mg/kg/j
- Pas de différence de mortalité à 10s



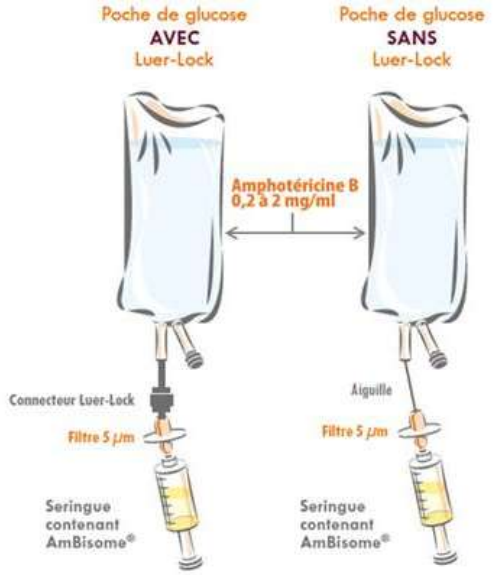
	Cohorte	Essai AMBITION
Durée d'hospitalisation	11j [7-14]	Non détaillée > 7j
Nb de PL	2 [1-3]	3
Dates des PL	J1, J3	J1, J7, J14
Suivi biologique	50% avec 1 BS	/3j pendant 14j
Effets indésirables grade 3-4	4% (2%?)	50%

Incidence des effets indésirables non comparable (différence de suivi biologique)

Gakaru *et al.*, Clin Infect Dis 2025

Précautions d'administration

- L-AmB :
  - Respecter la dose test d'1mg sur 20-30 minutes
  - Prescription d'accompagnement : paracétamol 1g +/- Polaramine 5mg IV +/- Hydrocortisone 25mg
  - A passer sur 2h minimum (attention à agiter chaque heure)
  - Apports hydrosodés et potassium



- 5-FC : à adapter à la fonction rénale + suivi thérapeutique pharmacologique

eGFR (mL/min)	21-40	10-20	<10
Dose	25 mg/kg/12h	25 mg/kg/24h	25 mg/kg/48h

Induction : surveillance

Monodose de L-AmB

Day	1	2	3	4	5	6	7	8
Single high-dose liposomal amphotericin B								
Pre-emptive hydration and electrolyte supplementation (adults and adolescents)								
1 litre of normal saline solution with 20 mEq KCl over two hours before infusion	X							
8-mEq KCl tablets orally (twice daily)	X	X	X					
Magnesium supplementation if available[a]	X	X	X					
Monitoring (adults, adolescents and children)								
Serum potassium	X		X					
Serum creatinine	X		X					
Haemoglobin	X						X[b]	

AmB désoxycholate 7 jours

Day	1	2	3	4	5	6	7	8	9
Amphotericin B deoxycholate: seven days									
Pre-emptive hydration and electrolyte supplementation (adults and adolescents)									
1 litre of normal saline solution with 20 mEq KCl over two hours before each controlled infusion	X	X	X	X	X	X	X		
2 times 8-mEq KCl tablet (twice daily)	X	X	X	X	X	X	X		
Magnesium supplementation if available[a]	X	X	X	X	X	X	X		
Monitoring (adults, adolescents and children)									
Serum potassium	X		X		X		X		X[b]
Serum creatinine	X		X		X		X		
Haemoglobin	X						X		

World Health Organization

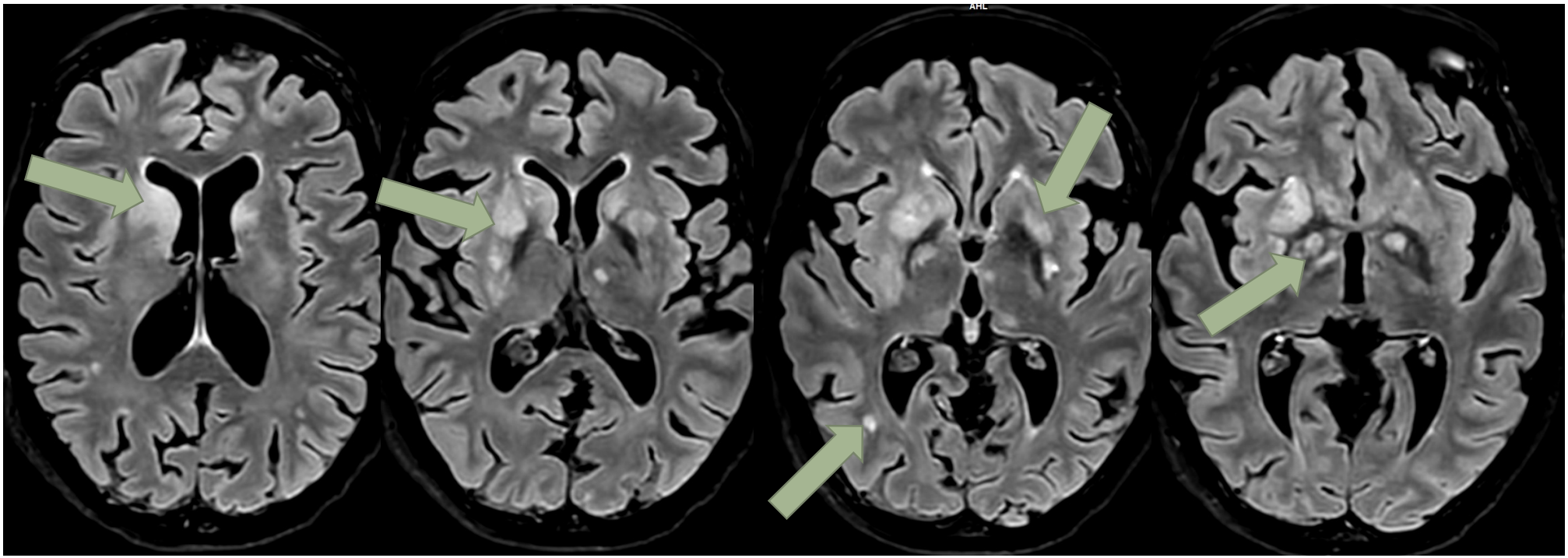
WHO 2022

Imagerie

Panel 8: **Recommendations for raised intracranial pressure**

- (AIIu) Opening pressure should be measured at every lumbar puncture in patients with cryptococcal meningitis
- (AIII) A brain CT should be done (if CNS imaging not already done) to exclude CNS outflow obstruction

- PL :
  - Si pression normale à J0 : J3-J7
  - Si pression élevée, PL quotidienne



Séquence T2 FLAIR – patiente de 46 ans, découverte de VIH, 24 CD4/mm^3

Merci à Julien Ognard, radiologue CHU Brest

Quand initier les ARV ?

Panel 9: Recommendations for the timing of ART commencement

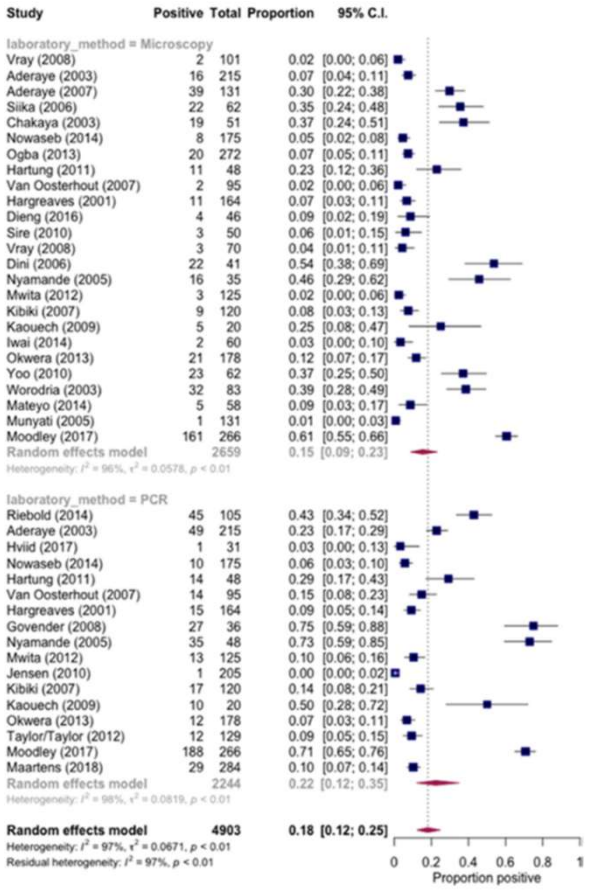
- (DI) Immediate or very early commencement of ART is not recommended.
- (AI) If suboptimal antifungal induction therapy is used, delay ART for 4–6 weeks.
- (BIIu) If optimal antifungal induction therapy was used, consider further individualisation, taking into consideration resolution of symptoms and signs of cryptococcal meningitis, intracranial pressure (including normalisation of opening pressure), attainment of CSF cryptococcal sterility, successful identification, management of concurrent co-infections and other AIDS-defining illnesses, the patient's readiness for ART, and local experience of cryptococcal meningitis and C-IRIS management (usual range is 4–6 weeks).
- (CIIt) If possible, ensure CSF is cryptococcal culture negative before ART commencement.
- (BIII) For people who have had ART who develop cryptococcal meningitis and might need to switch to second-line ART or recommence ART, a delay of 4–6 weeks is recommended.
- (CIII) Pending further studies, consider withholding ART and restarting at 4–6 weeks in those presenting with cryptococcal meningitis within 2 weeks of starting ART.
- (BIII) Patients with isolated pulmonary cryptococcosis or those with asymptomatic cryptococcal antigenemia can commence ART earlier (eg, at 2 weeks).

- Recommandations : différer l'introduction de 4-6 semaines
  - Plusieurs essais randomisés montrant une surmortalité si ARV débutés dans les 4 premières semaines

- A noter :
  - Essais faits avec des protocoles d'induction sans 5-FC ni L-AmB
  - étude rétrospective sur 190 patients issus de cohortes européennes/nord-américaines : pas de surmortalité si ARV débutés dans les 14 jours

Makadzange *et al.*, Clin Infect Dis 2010
Bisson *et al.*, Clin Infect Dis 2013
Ingle *et al.*, Clin Infect Dis 2023

Pneumocystose



ISHAM INTERNATIONAL SOCIETY FOR HUMAN AND ANIMAL MYCOLOGY

Medical Mycology, 2021, 59, 802–812
https://doi.org/10.1093/mmy/myab002
Advance Access Publication Date: 12 February 2021
Original Article

Original Article

The prevalence of laboratory-confirmed *Pneumocystis jirovecii* in HIV-infected adults in Africa: A systematic review and meta-analysis

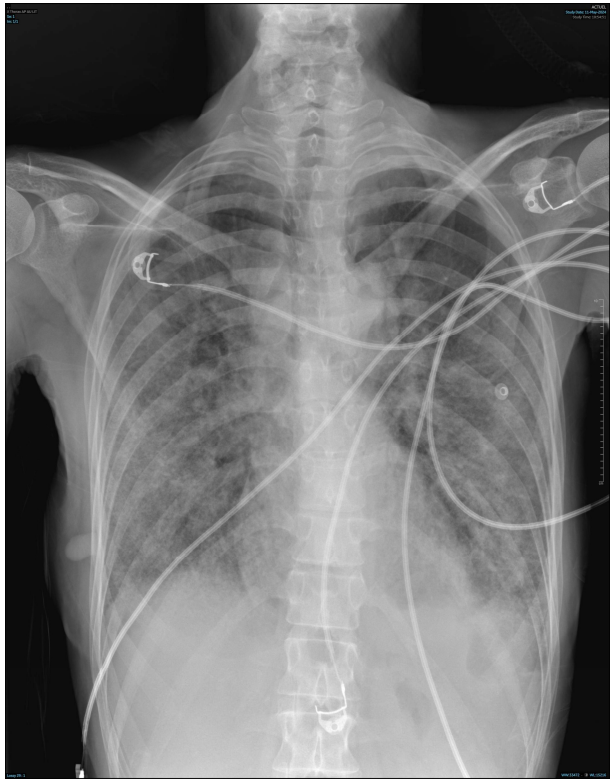
Nicola K. Wills[1,2,3,*], David S. Lawrence[2,4], Elizabeth Botsile[5], Mark W. Tenforde[6,7] and Joseph N. Jarvis[2,4]

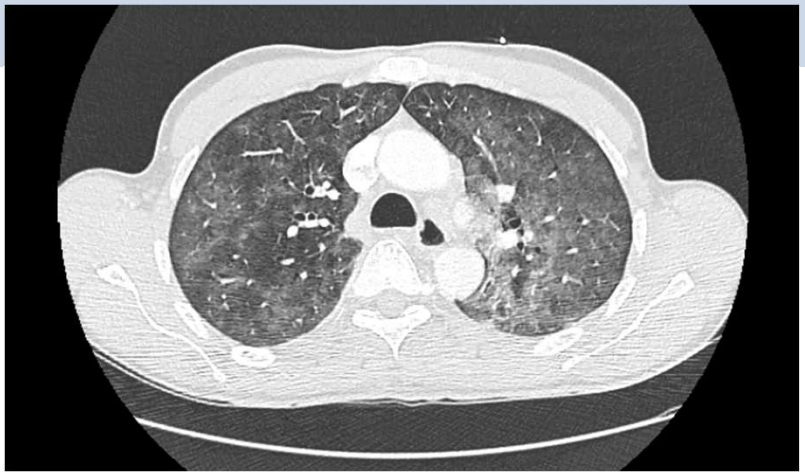
- *Pneumocystis jiroveci* : champignon atypique
  - Paroi contenant du cholestérol (≠ ergostérol)
  - Parasitisme stricte, spécificité de l'hôte
- Transmission : interhumaine, réactivation, environnement
- Prévalence (PVVIH en Afrique) :
  - Selon PCR : 22%
  - Selon ED : 15%

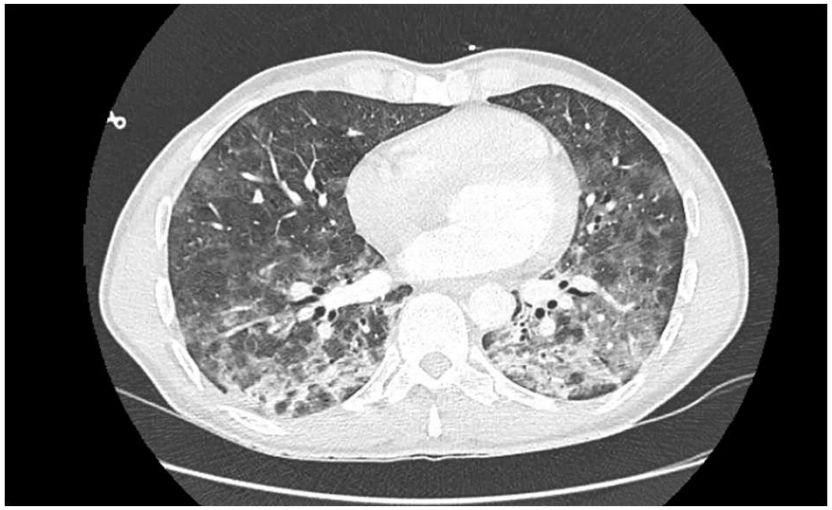
Wills *et al.*, Med Mycol 2021

Pneumocystose

- Intérêt de l'imagerie ++







Homme de 28 ans, découverte de VIH

Diagnostic clinique ?

Southern African Journal of HIV Medicine
ISSN: (Online) 2078-6751, (Print) 1608-9693
AOSIS
Page 1 of 6 Original Research

Development of a clinical prediction rule to diagnose *Pneumocystis jirovecii* pneumonia in the World Health Organization's algorithm for seriously ill HIV-infected patients

Authors:
Gary Maartens[1]
Annemie Stewart[1]
Rulan Griesel[1]
Andre P. Kengne[2]
Felix Dube[3,4]
Mark Nicol[3,4]
Molebogeng X. Rangaka[5,6,7]
Marc Mendelson[8]

- Développement d'un algorithme diagnostique clinique à partir d'une cohorte de patients avec PCR sur LBA > 1000 copies/mL
- Critère d'entrée : toux

TABLE 4: Clinical prediction rules derived from the respiratory rate and oxygen saturation multivariable logistic regression models for the diagnosis of *Pneumocystis jirovecii* pneumonia among 500 seriously ill HIV-infected participants presenting with a cough of any duration and one or more World Health Organization danger signs.

Variable	Points
Respiratory rate model	
Chest X-ray possible/likely PJP	2
Haemoglobin ≥ 9 g/dL	1
Respiratory rate 30–39	1
40–49	2
≥ 50	3
Oxygen saturation model	
Chest X-ray possible/likely PJP	3
Haemoglobin ≥ 9 g/dL	1
Saturation < 94%	2

PJP, *Pneumocystis jirovecii* pneumonia.

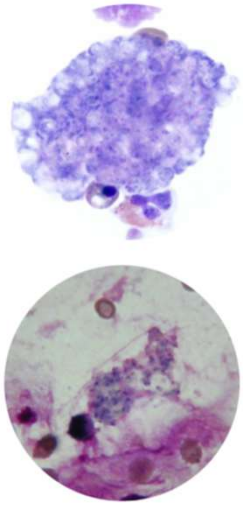
- Modèle sur la FR:

Total score	Number with score	Probability of PJP	Sensitivity	Specificity
Respiratory rate model				
0	50	0	100.0%	0.0%
1	153	3.1%	94.6%	10.6%
2	154	6.5%	82.1%	43.5%
3	73	13.3%	69.6%	76.6%
4	45	25.2%	51.8%	90.8%
5	23	42.5%	26.8%	97.8%
6	2	61.9%	1.8%	99.8%

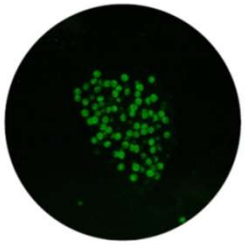
Maartens *et al.*, South Afr J HIV Med 2018

Diagnostic

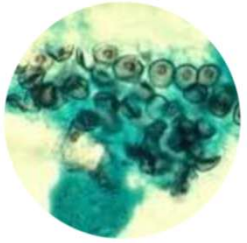
- Examen direct :
  - Giemsa
  - Immunofluorescence
  - Coloration argentique Gomori-Grocott
- Beta-D-glucane sur sang
  - Manque de spécificité
  - Bonne sensibilité chez les PVVIH
- qPCR : très bonne sensibilité et VPN
  - Sur LBA > sur crachat induit > aspiration nasopharyngée
  - Cut-off infection-colonisation?



Giemsa



Immunofluorescence

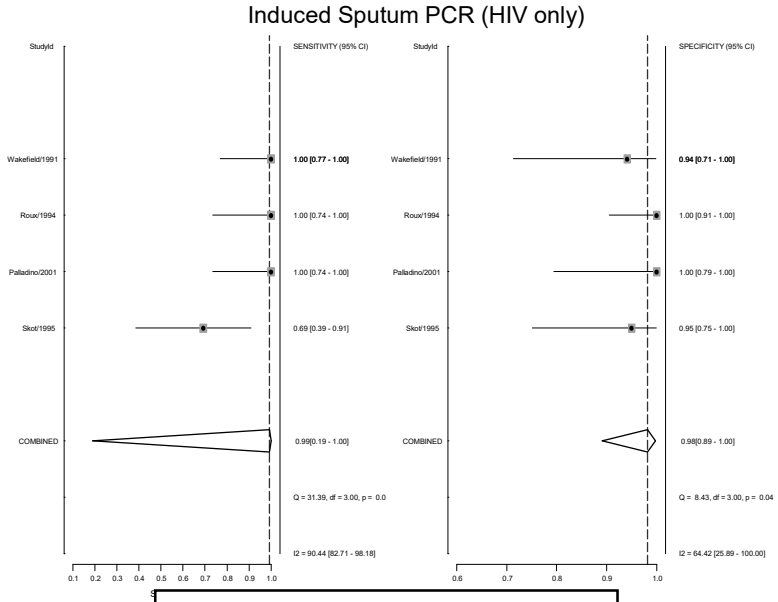


Coloration argentique Gomori-Grocott

Diapositive de Sarah Dellière, APHP

Crachat induit

- Une alternative acceptable au LBA ?
  - Surtout si qPCR ++
  - Sensibilité de la cytologie : 0,5 (0,39-0,61)



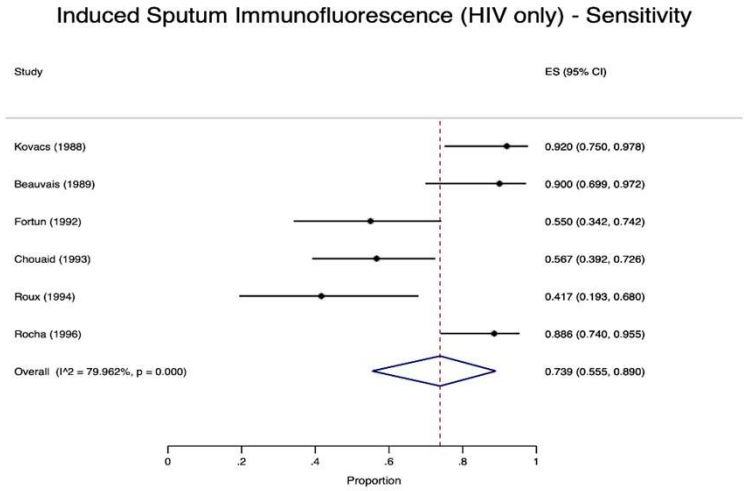
Sensibilité : 0,99 (0,19-1)
Spécificité : 0,98 (0,89-1)

Contents lists available at ScienceDirect
Clinical Microbiology and Infection
journal homepage: www.clinicalmicrobiologyandinfection.com

Systematic review

Non-invasive diagnosis of *Pneumocystis jirovecii* pneumonia: a systematic review and meta-analysis

Julien Senécal [1], Elizabeth Smyth [2], Olivier Del Corpo [1], Jimmy M. Hsu [1], Alexandre Amar-Zifkin [3], Amy Bergeron [3], Matthew P. Cheng [2, 4, 5], Guillaume Butler-Laporte [4, 6], Emily G. McDonald [2, 7, 8], Todd C. Lee [2, 4, 6, 7, *]



Sensibilité : 0,74 (0,56-0,89)
Spécificité : 1 (0,999-1)

Aspiration nasopharyngée : sensibilité 0,95 (0,73-1)

Sénécal *et al.*, Clin Microbiol Infect 2022

Prophylaxie primaire : chez qui ?

- Recommandations EACS et françaises :

CD4 count threshold / indication
CD4 count < 200 cells/µL, CD4 percentage < 14%, recurrent oral thrush, or relevant concomitant immunosuppression*
Prophylaxis against *Pneumocystis jirovecii* Pneumonia (PcP) & *Toxoplasma gondii* infection **Stop:** if CD4 count > 100 cells/µL and HIV-VL undetectable over 3 months * e.g. use of corticosteroids > 20 mg prednisone equivalent per day for > 2 weeks, cancer chemotherapy, biological agents such as rituximab Decisions on installation and discontinuation in these situations have to be taken individually

EACS European AIDS Clinical Society

- Recommandations IDSA :
  - A maintenir tant que CD4 < 200/mm^3
  - Considérer l'arrêt si CD4> 100/mm^3 et CV indétectable depuis ≥ 3 mois

Prophylaxie primaire : comment ?

- Cotrimoxazole ++
- Alternatives :

	Drug	Dose	Comments
Positive or negative serology for Toxoplasmosis	**trimethoprim-sulfamethoxazole (TMP-SMX)**	80/400 mg qd po or 160/800 mg qd po or 160/800 mg x 3/week po	In case of non-severe TMP-SMX allergy and if other therapeutic options are not available/not clinically appropriated, desensitization can be attempted*
Negative serology for toxoplasmosis	**pentamidine**	300 mg in 6 mL sterile water x 1 inhalation/month	Does not prevent the rare extrapulmonary manifestations of *P. jirovecii*
Negative serology for toxoplasmosis	**dapsone**	100 mg qd po	Check for G6PD-deficiency
Negative serology for toxoplasmosis	**atovaquone suspension**	1500 mg qd (with food)	
Positive serology for toxoplasmosis	**dapsone** **+ pyrimethamine** **+ folinic acid**	200 mg/week po 75 mg/week po 25-30 mg/week po	Check for G6PD-deficiency
Positive serology for toxoplasmosis	**atovaquone suspension** **+/- pyrimethamine** **+ folinic acid**	1500 mg qd po (with food) 75 mg/week po 25-30 mg/week po	

EACS European AIDS Clinical Society

HAS

Prophylaxie primaire

Contents lists available at ScienceDirect

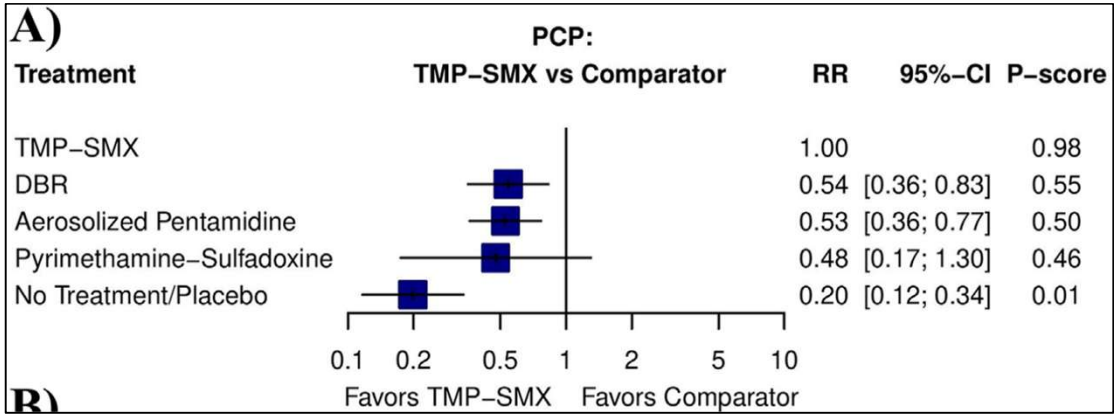
Clinical Microbiology and Infection

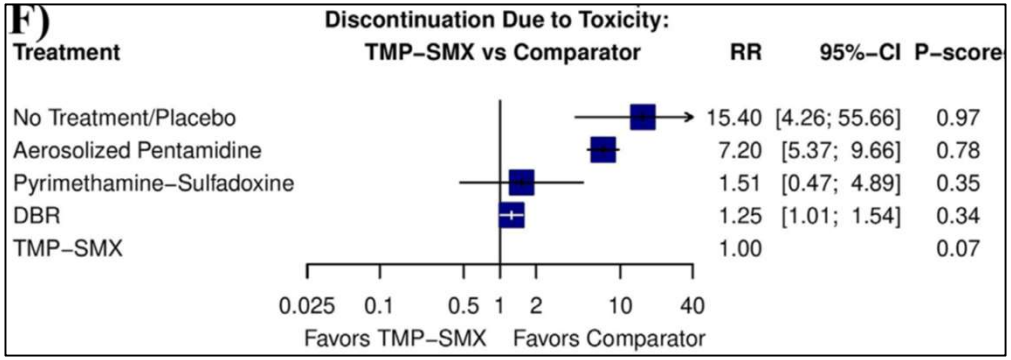
journal homepage: www.clinicalmicrobiologyandinfection.com

Systematic review

Comparative efficacy and safety of *Pneumocystis jirovecii* pneumonia prophylaxis regimens for people living with HIV: a systematic review and network meta-analysis of randomized controlled trials

Connor Prosty [1,*], Khaled Katergi [2], Mark Sorin [1], Marianne Bou Rjeily [1], Guillaume Butler-Laporte [3], Emily G. McDonald [4,5,6], Todd C. Lee [3,5,6]





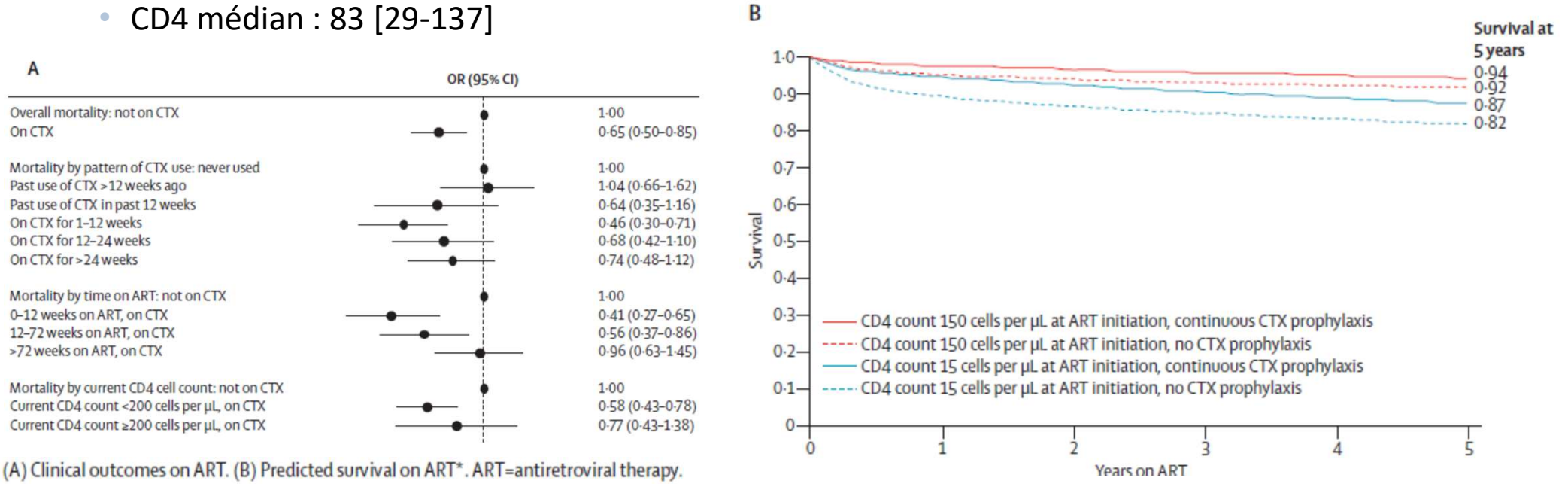
Prosty *et al.*, Clin Microbiol Infect 2024

Prophylaxie primaire

Daily co-trimoxazole prophylaxis in severely immunosuppressed HIV-infected adults in Africa started on combination antiretroviral therapy: an observational analysis of the DART cohort

A S Walker, D Ford, C F Gilks, P Munderi, F Ssali, A Reid, E Katabira, H Grosskurth, P Mugyenyi, J Hakim, J H Darbyshire, D M Gibb, A G Babiker

- Cohorte observationnelle sur 3179 participants de l'essai DART (Ouganda et Zimbabwe)
  - CD4 médian : 83 [29-137]



(A) Clinical outcomes on ART. (B) Predicted survival on ART*. ART=antiretroviral therapy.

- Réduction de la mortalité toutes causes : OR=0,65 (0,5-0,85)
- Réduction de la fréquence du paludisme : OR=0,74 (0,63-0,88)

Walker *et al.*, Lancet 2010

Prophylaxie primaire

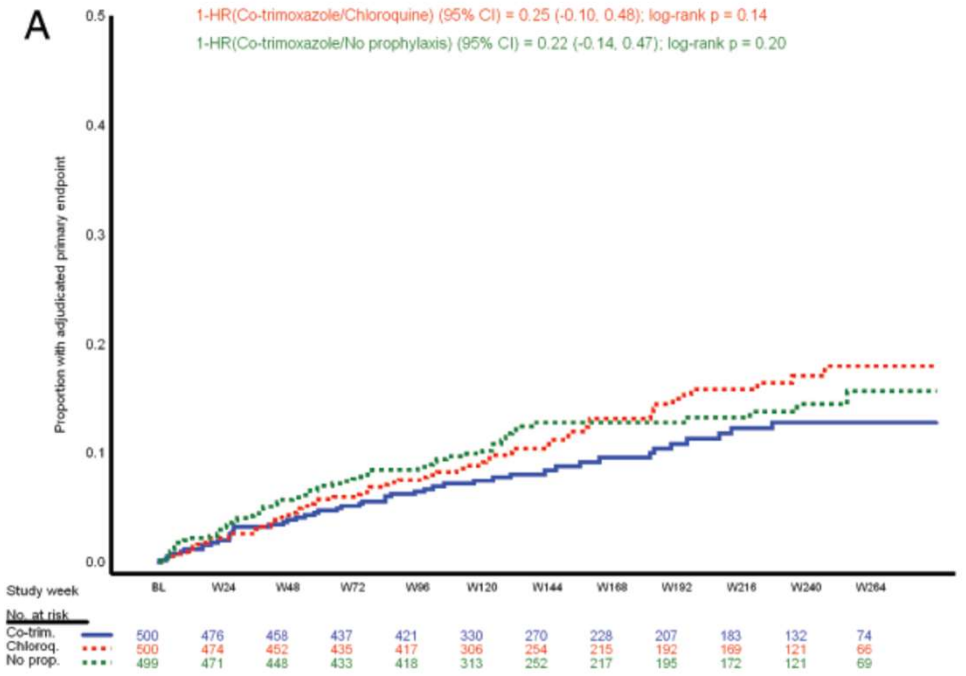
- Essai randomisé au Malawi
- Patients avec CD4>250/mm^3 et CV indétectable
- prévalence *P. falciparum* chez l'enfant : 26%)

- Incidence décès ou VIH stade 3-4 (WHO) :
  - Cotrimoxazole vs arrêt : HR = 0,75 (0,52-1,1)
  - → non significatif

Clinical Infectious Diseases
MAJOR ARTICLE

Revisiting Co-trimoxazole Prophylaxis for African Adults in the Era of Antiretroviral Therapy: A Randomized Controlled Clinical Trial

Matthew B. Laurens,[1,©] Randy G. Mungwira,[2,a] Nginache Nampota,[2] Osward M. Nyirenda,[2] Titus H. Divala,[2,b] Maxwell Kanjala,[2] Felix A. Mkandawire,[2] Lufina Tsirizani Galileya,[2] Wongani Nyangulu,[3] Edson Mwinjiwa,[3] Matthew Downs,[4] Amy Tillman,[4] Terrie E. Taylor,[2,5] Jane Mallewa,[2] Christopher V. Plowe,[1] Joep J. van Oosterhout,[6,c] and Miriam K. Laufer[1]



Laurens *et al.*, Clin Infect Dis 2021

Traitement

- 1ère intention : consensus
  - Cotrimoxazole : 15/75 mg/kg/j en 3 prises pendant 21 jours
  - Associé à prednisone 40mg/12h pdt 5j, puis 40mg/j pdt 5j puis 20mg/j pdt 10j si PaO2 < 70 mmHg
  - Débuter les ARV dans les 2 semaines

- 2ème intention : absence de consensus
  - Primaquine + clindamycine (1er choix selon IDSA, recherche de déficit G6PD)
  - Pentamidine IV (si forme grave)
  - Atovaquone (si forme légère à modérée)

HAS EACS European AIDS Clinical Society CLINICAL INFO HIVgov

McDonald *et al.*, Clin Microbiol Rev 2024

Candidoses

- Incidence candidose oropharyngée : ~ 50% des PVVIH et 90% des patients au stade SIDA
- Recommandations françaises 2024 (= IDSA et EACS) :

Tableau 4 : Traitement curatif de la candidose oropharyngée et œsophagienne

	Candidose oropharyngée	Candidose œsophagienne
Première intention	fluconazole 200 mg en dose de charge, puis 100 mg/j 7 jours	fluconazole 400 mg en dose de charge, puis 200 mg/j PO (ou IV en cas de troubles de déglutition) 14 jours
Alternative	Formulation topique : – amphotéricine B suspension orale 1-2 g, 2-4x/j – miconazole un comprimé muco-adhésif à appliquer sur la gencive 1x/j	Ne pas utiliser les formulations topiques
Si échec, après réalisation de prélèvements microbiologiques :	– posaconazole en suspension 100 mg x2/j – voriconazole 200mg x2/j – isavuconazole 200 mg en dose de charge, puis 50 mg/j [hors AMM] – échinocandine (caspofungine [hors AMM], micafungine)	

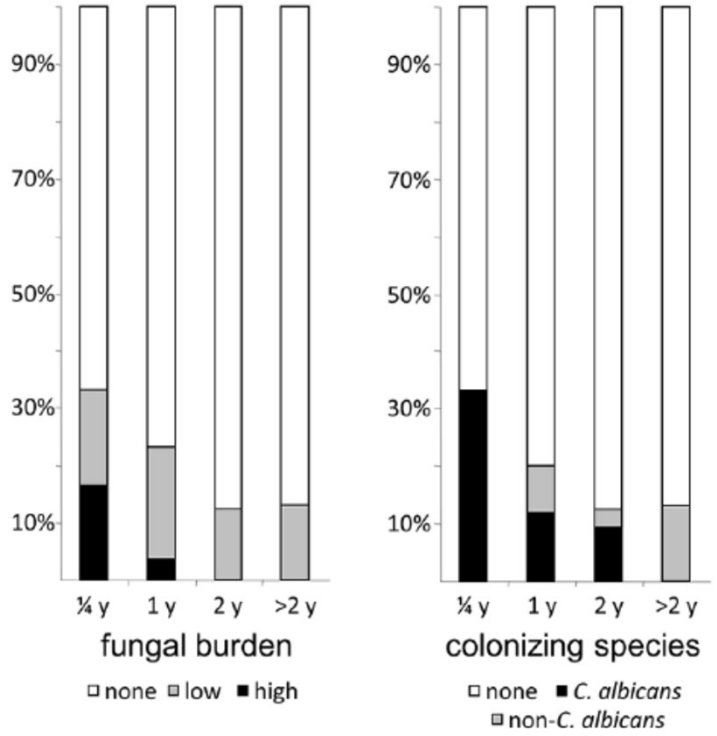
HAS

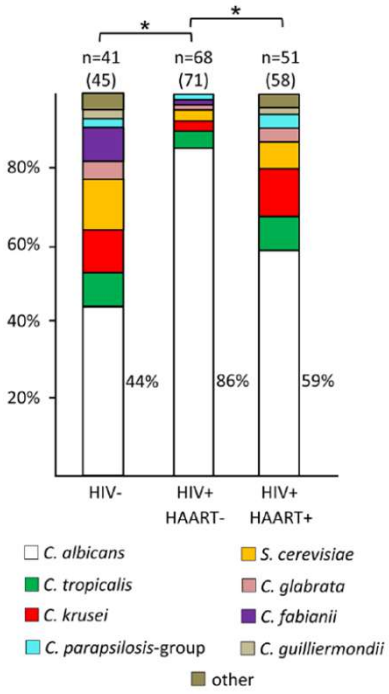
Candidoses

Epidemiology and Prevalence of Oral Candidiasis in HIV Patients From Chad in the Post-HAART Era

Liliane Taverne-Ghadwal[1], Martin Kuhns[1], Timo Buhl[2], Marco H. Schulze[1], Weina Joseph Mbaitolum[3], Lydia Kersch[4], Michael Weig[1], Oliver Bader[1†] and Uwe Groß[1†]*

- Etude prospective chez 589 patients (dont 384 PVVIH) au Chad : 1 centre VIH et 1 centre rural





- Prévalence candidose orale : 16% chez PVVIH non traité et 2% chez PVVIH traité, p<0,02
- Les ARV réduisent la colonisation fongique

Taverne-Ghadwal *et al.*, Frontiers in Microbiol 2022

Résistances

Journal of Fungi

MDPI

Article

Fluconazole Resistance among Oral *Candida* Isolates from People Living with HIV/AIDS in a Nigerian Tertiary Hospital

Iriagbonse I. Osaigbovo [1,2,*], Patrick V. Lofor [1,2] and Rita O. Oladele [3]

- Etude prospective chez 700 patients au Nigeria
- PVVIH : 21% de cultures positives vs non-VIH : 3% (p<0,001)
- Chez les PVVIH :
  - *C. albicans* = 83% des isolats, dont 24% de résistance au fluconazole
  - Autres espèces : 50% de résistance

Table 2. Factors associated with fluconazole resistant isolates in PLWHA.

Variable	Resistant Isolate *n* = 18	Sensitive/S-DD [1] Isolate *n* = 57	χ^2	*p*-Value
Past Fluconazole Use				
Present	16 (48.5)	17 (51.5)	19.368	<0.001
Absent	2 (4.8)	40 (95.2)		
History of OPC				
Present	13 (41.9)	18 (58.1)	9.319	0.002
Absent	5 (11.4)	39 (88.6)		
Species				
C. albicans	11 (18.0)	50 (82.0)	NA [2]	0.032
NAC	7 (50.0)	7 (50.0)		

[1] S-DD = susceptible dose-dependent; [2] NA = not applicable, Fisher's Exact Test used; Percentages in parentheses represent row variable.

Osaigbovo *et al.*, J of Fungi 2017

Candida auris

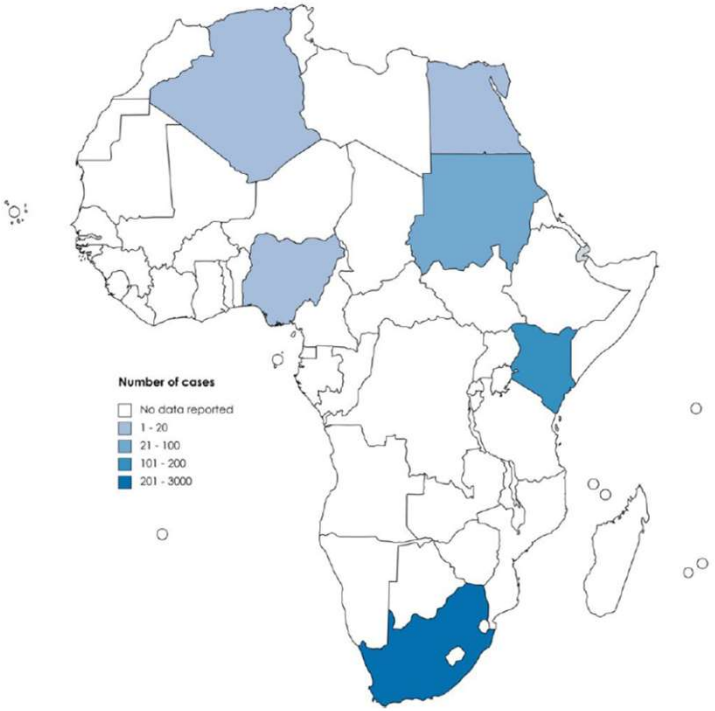
- Pathogène émergent décrit en 2009
- Plusieurs clades différents
- Epidémies nosocomiales
- Absence de cas décrit chez PVVIH

- Revue systématique (19 études)
- 2529 cas, dont 94% en Afrique du Sud
- Résistances :
  - 91% au FCZ
  - 21 à l'AmB
  - 2% aux échinocandines

Open Forum Infectious Diseases
REVIEW ARTICLE

Candida auris: A Systematic Review of a Globally Emerging Fungal Pathogen in Africa

Iriagbonse I. Osaigbovo,[1,2] Bassey E. Ekeng,[3] Adeyinka A. Davies,[4] Ejime Ebeigbe,[2] Felix Bongomin,[5,6] Alice Kanyua,[7] Gunturu Revathi,[7] and Rita O. Oladele[8]



Osaigbovo *et al.*, Open Forum Infect Dis 2024

Take-home messages

- Cryptococcose :
  - Induction : L-AmB monodose + FCZ + 5-FC
    - Efficacité similaire
    - Meilleure tolérance
  - Screening AgCr chez PVVIH < 100 CD4/mm^3 voir < 200 CD4/mm^3
- Pneumocystose :
  - Accessibilité aux méthodes diagnostiques (PCR, TDM)
  - Prophylaxie par Cotrimoxazole chez PVVIH < 200 CD4/mm^3 jusqu'à > 200 CD4/mm^3
- Candidoses :
  - Intérêt de l'antifongigramme si échec

Dans tous les cas, intérêt ++ des ARV

Merci pour votre attention