Best of
Infections fongiques invasives

Alexandra Serris
Service de maladies infectieuses et tropicales
Hôpital Necker-enfants malades

Candida

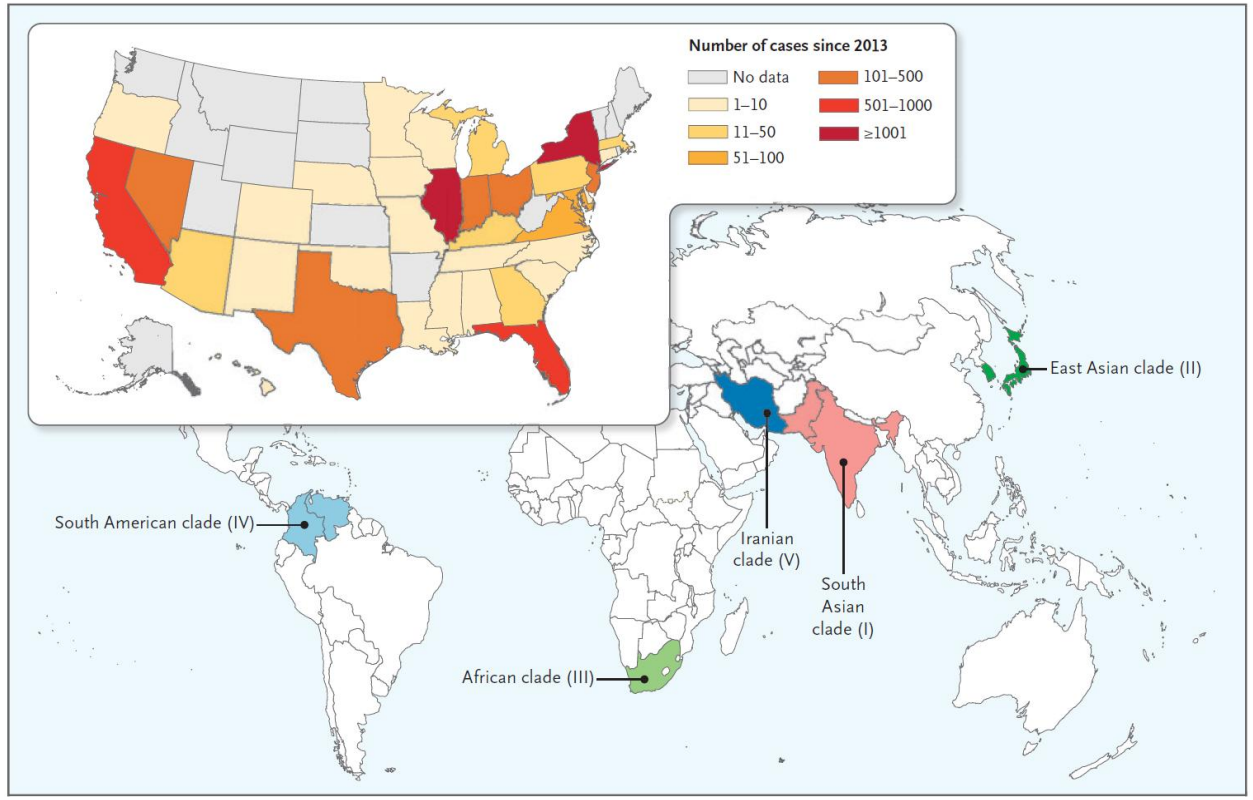
The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

C. Corey Hardin, M.D., Ph.D., *Editor*

Candida auris Infections

Michail S. Lionakis, M.D., Sc.D., and Anuradha Chowdhary, M.D., Ph.D.



- Isolé au Japon en 2009 pour la première fois; émergence simultanée sur 6 continents, actuellement présent dans 45 pays
- Survit aux hautes températures et aux fortes concentrations en sel
  - Rupture de la « barrière d'endothermie » humaine
  - Adaptation liée au réchauffement climatique ?
- Persiste sur la peau et les surfaces pendant des périodes prolongées (biofilm)
  - Transmission nosocomiale importante

Lionakis *et al.* NEJM, 2024

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Candida auris Infections

Michail S. Lionakis, M.D., Sc.D., and Anuradha Chowdhary, M.D., Ph.D.

- La colonisation de la peau est un facteur de risque de candidémie :
  - 25% des patients en USI colonisés développent une candidémie

- Rapporté comme cause de :
  - myocardite, péricardite, méningite, infection hépatosplénique, ostéomyélite, infection urinaire, endophtalmie, otite, surinfection de blessures
  - Transmission par le greffon (transplantation pulmonaire)

- Résistance aux antifongiques
  - 90% de souches résistantes au fluconazole sauf clade II (Asie de l'Est)
  - 5% de souches résistantes aux échinocandines (mais en augmentation : x3 en 2021)

- Risque de rechute est plus élevé qu'avec les autres espèces de candida

Lionakis *et al.* NEJM, 2024

Rezafungin versus caspofungin for patients with candidaemia or invasive candidiasis in the intensive care unit: pooled analyses of the ReSTORE and STRIVE randomised trials

Critical Care

Patrick M. Honoré[1*], Massimo Girardis[2], Marin Kollef[3], Oliver A. Cornely[4,5,6], George R. Thompson III[7], Matteo Bassetti[8], Alex Soriano[9], Haihui Huang[10], Jose Vazquez[11], Bart Jan Kullberg[12], Peter G. Pappas[13], Nick Manamley[14], Taylor Sandison[15], John Pullman[16] and Saad Nseir[17]

Comparaison efficacité et tolérance de la rezafungine vs caspofungine en réanimation

- STRIVE et ReSTORE : essais contrôlés randomisés rezafungine vs caspofungine pour le traitement d'une candidémie ou candidose invasive
- Analyse des 113 patients hospitalisés en USI
  - analyse non prévue à priori donc groupes non strictement comparables
  - NB : 1 seul patient neutropénique

	rezafungine	**caspofungine**	**P**
Mortalité à 30 jours	35%	26%	ns
Clairance fongique à J5	78%	60%	ns
Clairance fongique à J14	72%	66%	ns
Temps médian avant négativation des hémocultures	18 j [13-43]	38 j [16-211]	0,001
Arrêt du traitement pour EI	17%	30%	ns

Honoré *et al.*, Crit Care, 2024

Clinical Infectious Diseases
MAJOR ARTICLE
IDSA Infectious Diseases Society of America · hivma hiv medicine association · OXFORD

Prosthetic Joint Infections due to *Candida* Species: A Multicenter International Study

Aurélien Dinh,[1] Martin McNally,[2] Emma D'Anglejan,[1] Christel Mamona Kilu,[1] Julie Lourtet,[3] Rosemary Ho,[2] Matthew Scarborough,[2] Maria Dudareva,[2] Gerald Jesuthasan,[2] Cecile Ronde Oustau,[4] Stéphane Klein,[4] Laura Escolà-Vergé,[5] Dolores Rodriguez Pardo,[5] Pierre Delobel,[6] Jaime Lora-Tamayo,[7] Mikel Mancheño-Losa,[7] Maria Luisa Sorlí Redó,[8] José María Barbero Allende,[9] Cédric Arvieux,[10] Danguole Vaznaisiène,[11] Thomas Bauer,[12] Anne-Laure Roux,[13] Latifa Noussair,[13] Stéphane Corvec,[14] Marta Fernández-Sampedro,[15] Nicolò Rossi,[16] Adrien Lemaignen,[17] Mauro José Costa Salles,[18] Taiana Cunha Ribeiro,[18] Julien Mazet,[19] Milène Sasso,[19] Jean-Philippe Lavigne,[19] Albert Sotto,[19] Etienne Canouï,[20] Éric Senneville,[21] Pauline Thill,[21] Olivier Lortholary,[22,23] Fanny Lanternier,[22,23] Laura Morata,[24] Alex Soriano,[24] Gérard Giordano,[25] Camille Fourcade,[26] Bernhard J. H. Frank,[27] Jochen G. Hofstaetter,[27] Clara Duran,[1] and Eric Bonnet[26]; for the European Society of Clinical Microbiology and Infectious Diseases Study Group on Implant Associated Infections (ESGIAI)[a]

Quel est le pronostic des infections articulaires sur prothèses à Candida ?

- Étude rétrospective, 246 patients
- Terrain : 90% de patients immunocompétents, patients multi-opérés
- Expression clinique indolente
- Co-infection bactérienne dans 50% des cas
- Guérison à 1 an : 58%. Facteurs de risque d'échec :
  - âge et absence de changement de prothèse
  - Meilleur pronostic des infections à *C. parapsilosis* (échec : 32%) vs *C. albicans* (échec : 48%)
  - Pas d'impact de l'immunosuppression, utilisation d'azolés ou de la durée du traitement (médiane : 3 mois)

Dinh *et al.*, CID, 2024

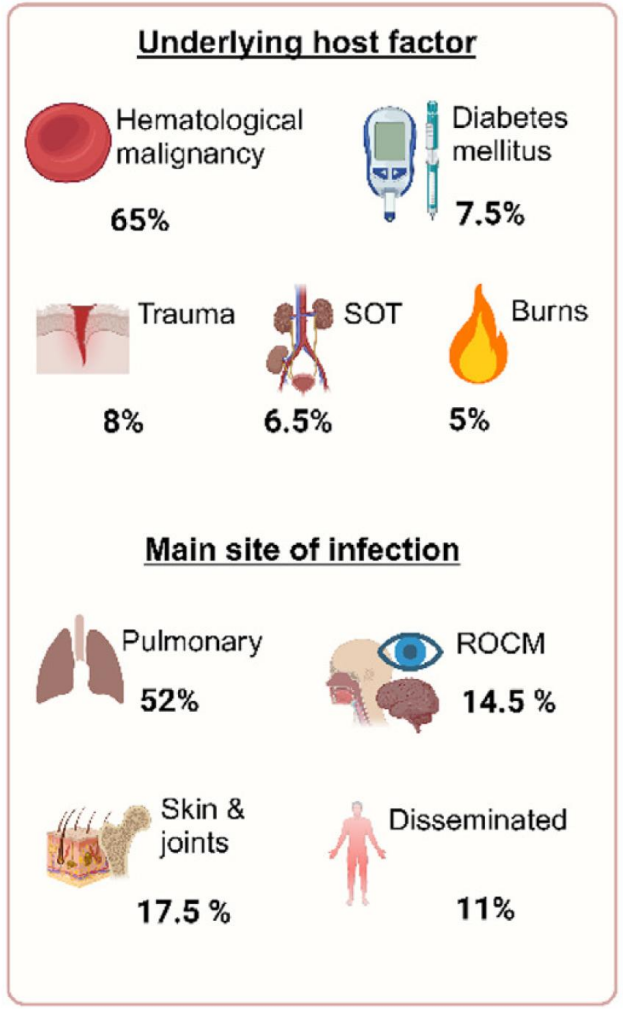
Mucorales

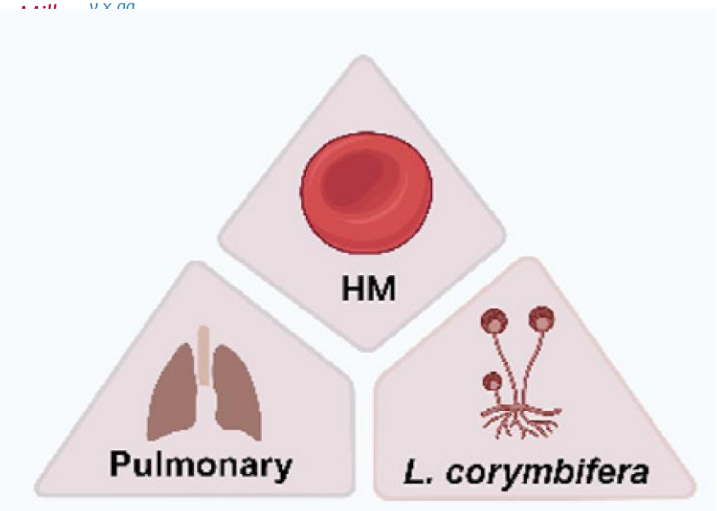
Epidemiology and prognostic factors of mucormycosis in France (2012–2022): a cross-sectional study nested in a prospective surveillance programme

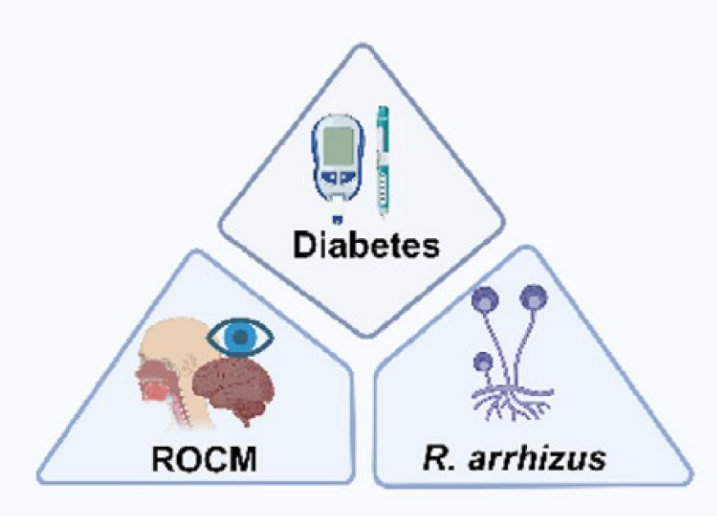
The Lancet Regional Health - Europe

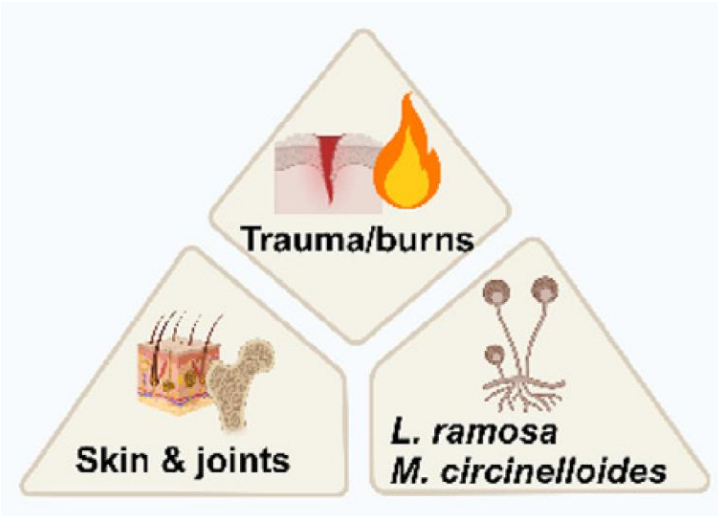
Laura Gouzien,[a,b] Didier Che,[c] Sophie Cassaing,[d,y] Olivier Lortholary,[a,e,y] Valérie Letscher-Bru,[f,g,y] Olivier Paccoud,[e] Thomas Obadia,[a,w] Florent Morio,[h] Maxime Moniot,[i] Estelle Cateau,[j] Marie Elisabeth Bougnoux,[k,l] Taieb Chouaki,[m] Lilia Hasseine,[n] Guillaume Desoubeaux,[o,p] Cecile Gautier,[a] Caroline Mahinc-Martin,[q] Antoine Huguenin,[r,s] Julie Bonhomme,[t] Karine Sitbon,[a] Julien Durand,[c] Alexandre Alanio,[a,u,aa] Laurenc
Dea Garcia-Hermoso,[a,z] and Fanny Lanternier,[a,e,*,z] the French Mycoses Study Group

- Etude française rétrospective
- 2012-2022
- 550 cas de mucormycose









Gouzien L. Lancet Reg Health Eur 2024;45:101010

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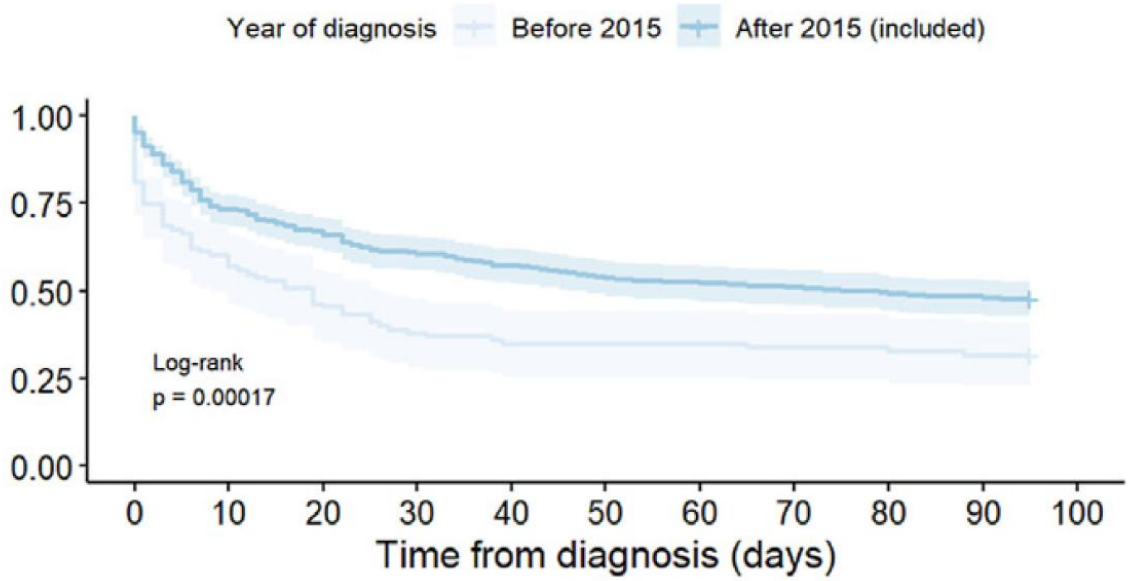
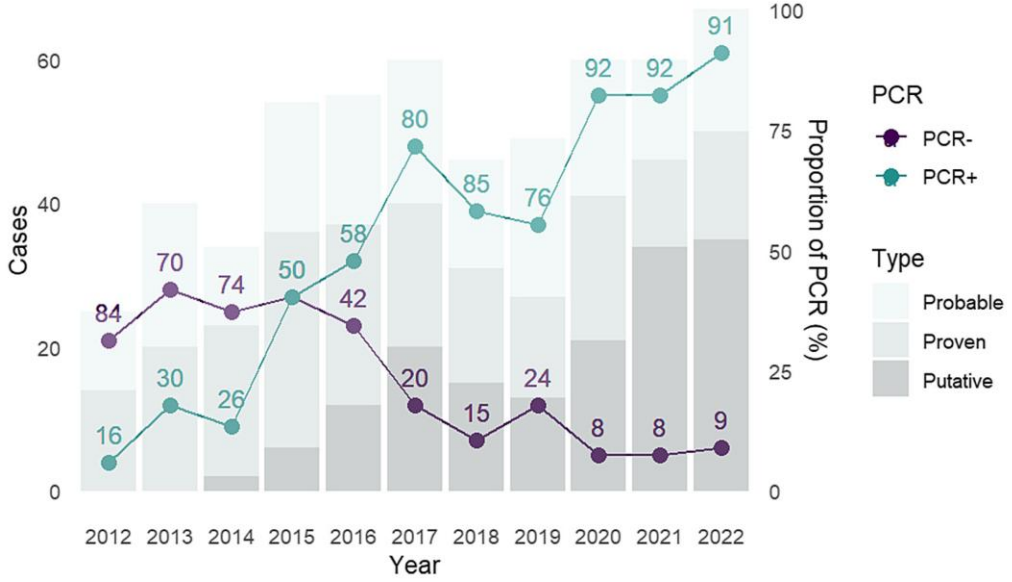




Factors associated with 90-day mortality

- Older age (per year): OR=**1.02** [1.01-1.03]
- Hematological malignancy : OR= **2.51** [1.73-3.66]
- ICU stay at diagnosis : OR = **3.25** [2.17-4.92]
- Trauma: OR = **0.17** [0.07-0.34]
- Diagnosis after 2015: OR = **0.51** [0.32- 0.82]
- Surgery: OR **0.23** [0.12–0.41]

90-day case fatality ratio: 55.8%

Gouzien L. Lancet Reg Health Eur 2024;45:101010

Pneumocystis

[Chest Infections Original Research] CHEST

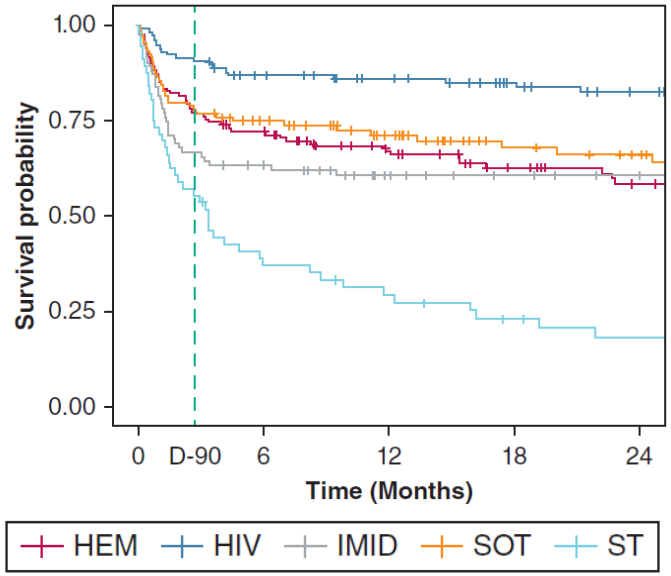
Characteristics and Prognosis Factors of *Pneumocystis jirovecii* Pneumonia According to Underlying Disease

A Retrospective Multicenter Study

Romain Lécuyer, MD, PharmD; Nahéma Issa, MD; Fabrice Camou, MD; Rose-anne Lavergne, PharmD, PhD; Frederic Gabriel, MD, PhD; Florent Morio, PharmD, PhD; Emmanuel Canet, MD, PhD; François Raffi, MD, PhD; David Boutoille, MD, PhD; Anne Cady, PharmD; Marie Gousseff, MD; Yoann Crabol, MD; Antoine Néel, MD, PhD; Benoît Tessoulin, MD, PhD; and Benjamin Gaborit, MD, PhD; and the PRONOCYSTIS Study Group*

Est-ce que le terrain et le type d'immunosuppression impactent la présentation clinique et le pronostic de la pneumocystose ?

- 481 patients ayant une PcP prouvée (ED+) ou probable (PCR +)
  - 114 HIV + / 367 HIV – (hémopathies malignes, TOS, maladies inflammatoires, cancers solides)
- Mortalité à 90 jours : 25,6%
- Seuls 10% des patients étaient sous prophylaxie
- 3 groupes associés à une plus grande mortalité à 90 jours :
  - cancers solides
  - maladies inflammatoires
  - corticoïdes surtout > 10 mg/j



Lécuyer *et al.*, Chest, 2024

[Chest Infections Original Research] CHEST

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Check for updates

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Maladies inflammatoires

- Polyarthritre rhumatoïde, vascularite à ANCA, sarcoïdose
- Délai court entre 1ers symptômes et hospitalisation
- Tableau plus sévère, Score SOFA élevé à l'admission / autre population VIH-
- Délai important entre admission et introduction d'un traitement

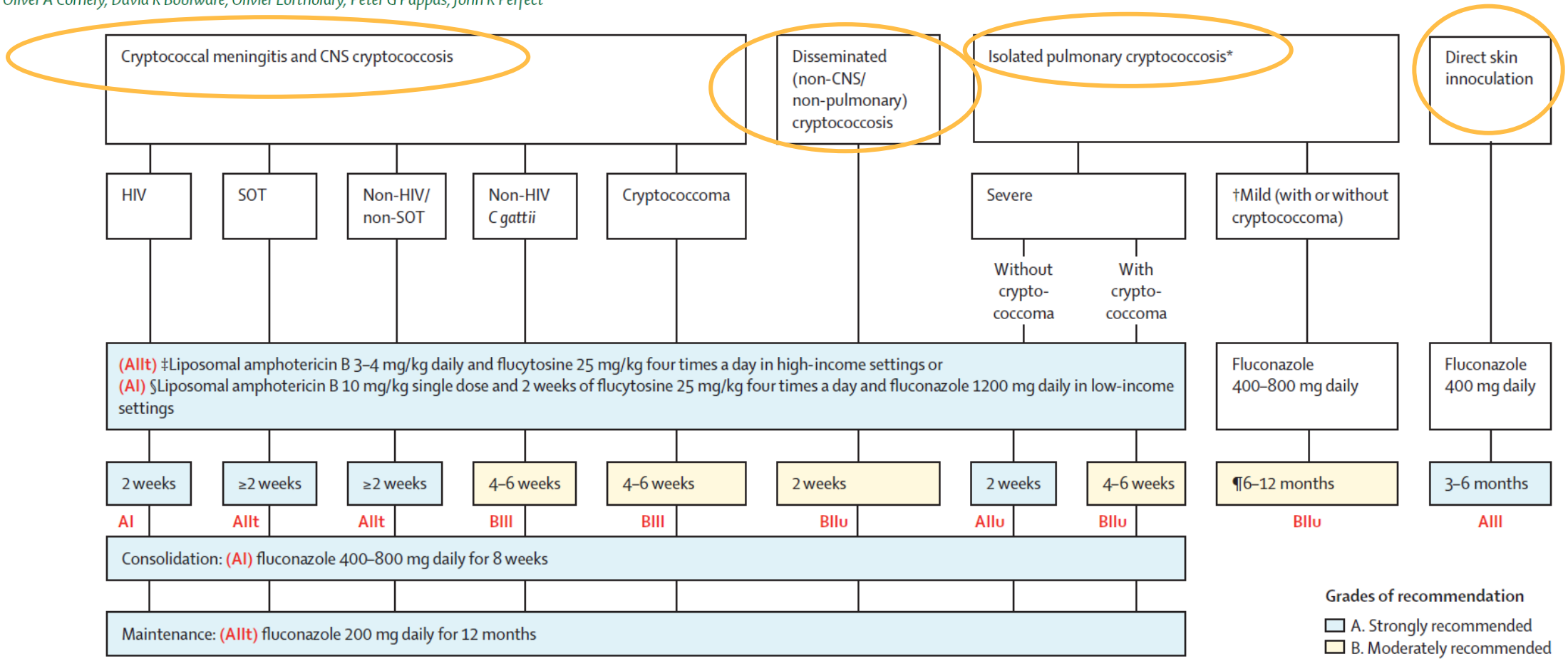
➢ Délai diagnostic responsable de l'augmentation de mortalité ?

Lécuyer *et al.*, Chest, 2024

Cryptococcoque

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, 2024

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

Panel 3: Recommendations for yeast causing cryptococcosis and diagnostic methods

(AIIt) All patients with suspected or confirmed cryptococcosis (including cryptococcal antigenemia) require clinical assessment for CNS, pulmonary, and other body site involvement.

Investigations for disseminated disease should include:

- Lumbar puncture with measurement of CSF opening pressure, glucose, protein, cell counts, microscopy, and culture and quantification of CSF cryptococcal antigen
- Quantification of blood cryptococcal antigen and cultures of blood, sputum (or other respiratory specimens), or other affected sites
- Brain imaging (preferably MRI) and chest imaging (preferably CT)

Chang *et al.*, Lancet, 2024

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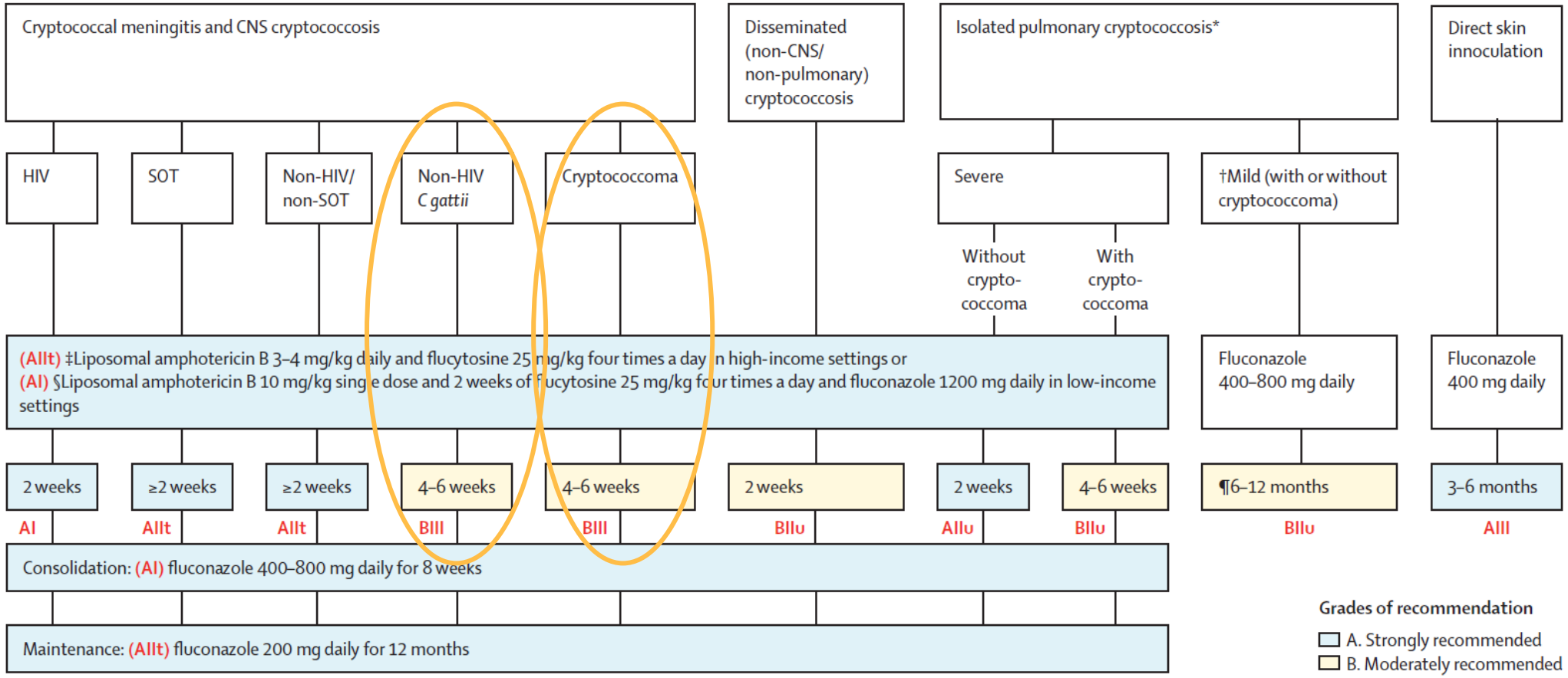

Chang *et al.*, Lancet, 2024

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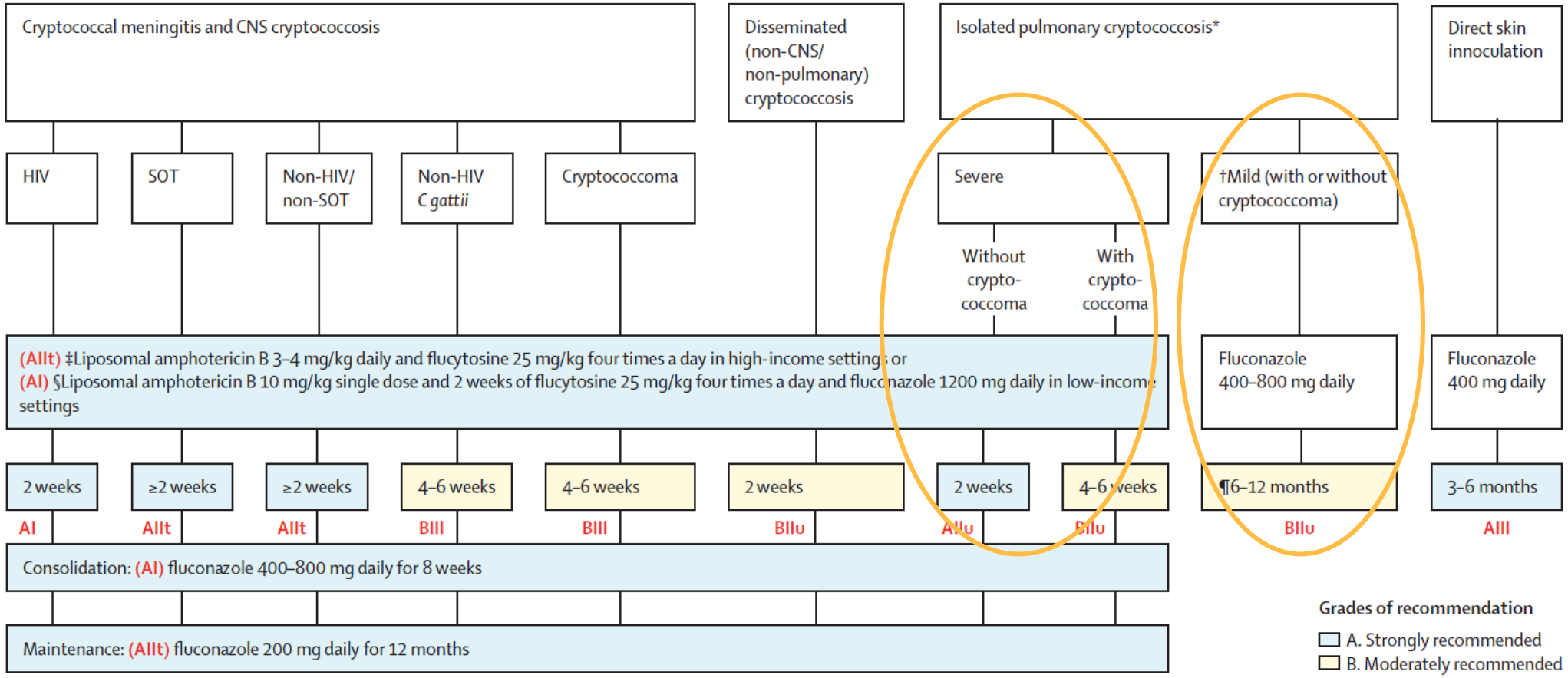

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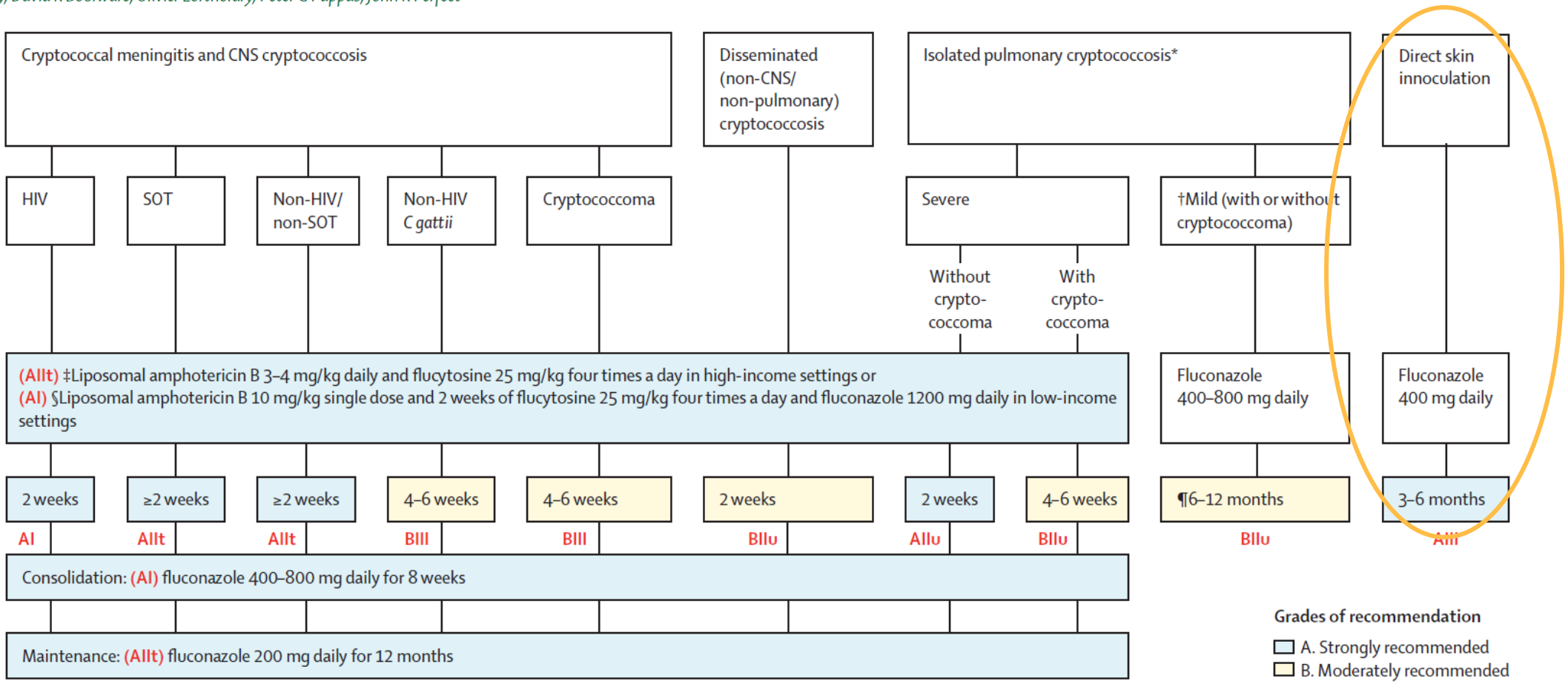
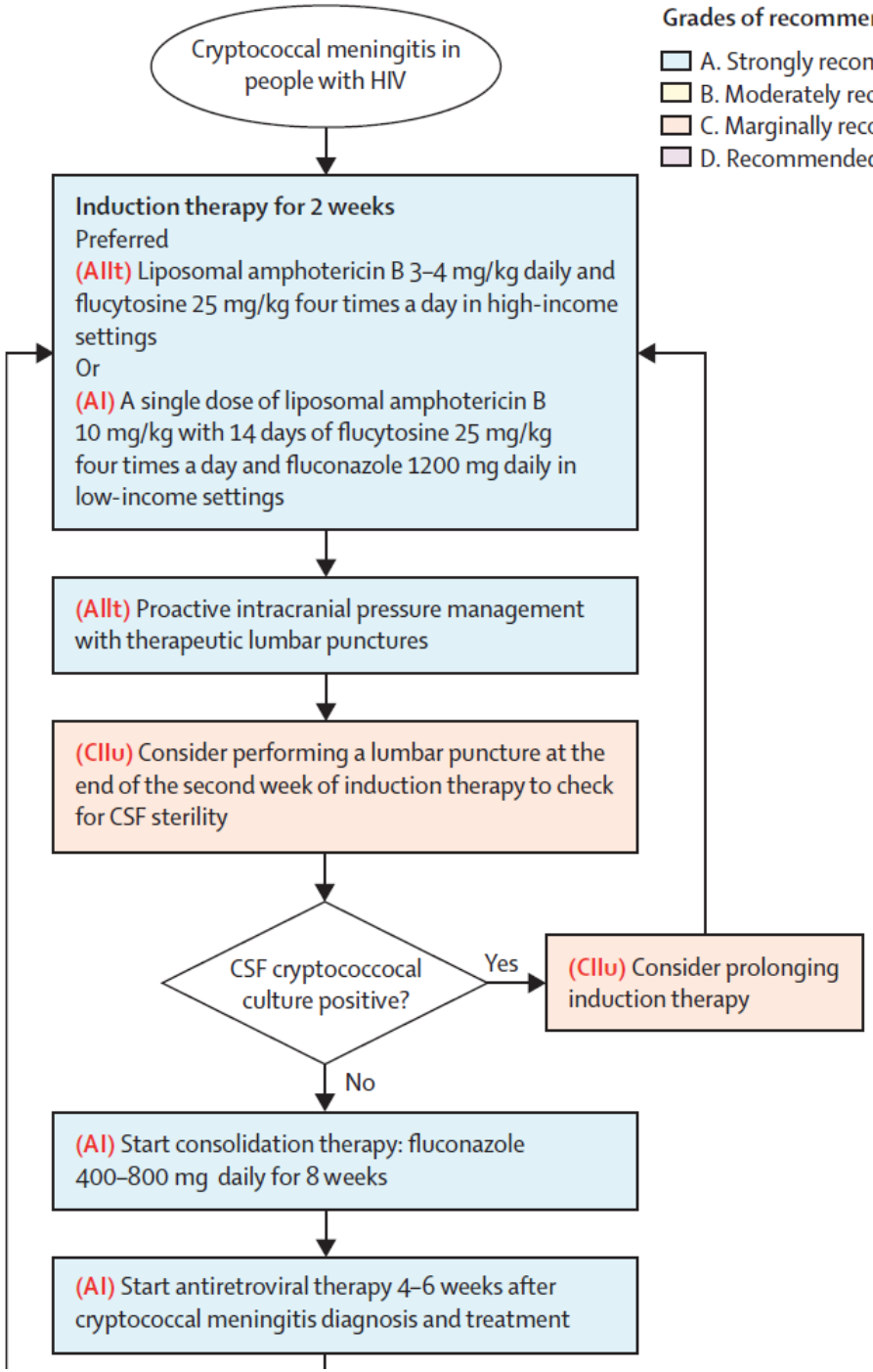


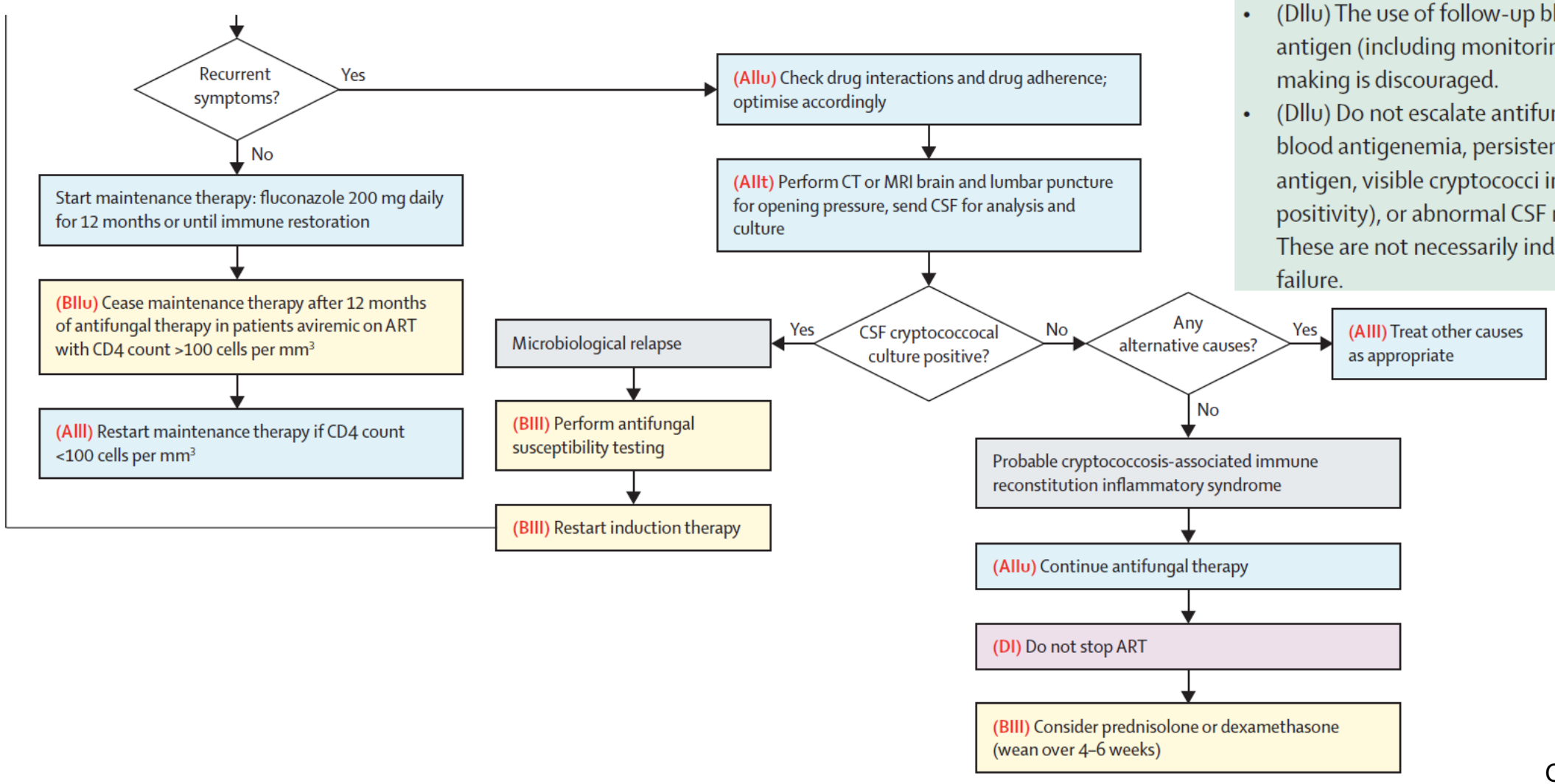
Chang *et al.*, Lancet, 2024



4) Manage raised intracranial pressure

- (AIIu) Opening pressure should be measured at every lumbar puncture in patients with cryptococcal meningitis.
- (AIIt) Acute symptomatic elevation of the intracranial pressure (≥20 cm of CSF) should be managed by daily therapeutic lumbar punctures (ie, removal of sufficient CSF, usually around 20–30 mL) to reduce the pressure to 50% of opening pressure or to a normal pressure of ≤20 cm of CSF (documented as a closing pressure).
- (BIIu) Perform a scheduled therapeutic lumbar puncture 48–72 h after initial lumbar puncture or 7 days, regardless of initial opening pressure.
- (AIIt) Persistent raised symptomatic intracranial pressure despite therapeutic lumbar punctures should be managed by surgical decompression via temporary lumbar drainage, shunting, or ventriculostomy, depending on local expertise and resources.

Chang *et al.*, Lancet, 2024



- (DIIu) The use of follow-up blood or CSF cryptococcal antigen (including monitoring of titres) for clinical decision making is discouraged.
- (DIIu) Do not escalate antifungal therapy for persistent blood antigenemia, persistently positive CSF cryptococcal antigen, visible cryptococci in CSF (without culture positivity), or abnormal CSF microscopy or biochemistry. These are not necessarily indicators of microbiological failure.

Chang *et al.*, Lancet, 2024

Management, Outcomes, and Predictors of Mortality of *Cryptococcus* Infection in Patients Without Human Immunodeficiency Virus: A Multicenter Study in 46 Hospitals in Australia and New Zealand

Get access

Julien Coussement, Christopher H Heath, Matthew B Roberts, Rebekah J Lane, Tim Spelman, Olivia C Smibert, Anthony Longhitano, C Orla Morrissey, Blake Nield, Monica Tripathy ... Show more

Clinical Infectious Diseases, ciae630, https://doi.org/10.1093/cid/ciae630

Pronostic des infections à cryptocoque chez les patients VIH – ? Quelles différences entre *C. neoformans* et *C. gattii* ?

426 patients without HIV diagnosed with cryptococcosis between 2015 and 2019 in Australia and New Zealand

Use of induction therapy:

- **Common in central nervous system cryptococcosis (99.5%, 192/193)**, typically with liposomal amphotericin + flucytosine (94%, 181/193), with mean duration 31 ± 13 days
- **27% of cases of isolated lung infection** (i.e., azole antifungal as 1st line treatment in 73%, 120/166)

Distinct outcomes of *C. gattii* infection:

(versus *C. neoformans*)

- **Lower mortality** (adjusted odds ratio: 0.47, 95% CI 0.23-0.95, all-cause 1-year mortality: 11% for *C. gattii* vs. 28% for *C. neoformans*)
- **Higher risk of immune reconstitution inflammatory response** (21% vs 3% in central nervous system infection, $p < 0.001$)

No microbiological relapses:

- **None of 19 patients who had re-induction with amphotericin-based therapy for suspected relapse had confirmed microbiological relapse** (i.e. positive culture)
- Central nervous system immune reconstitution inflammatory response seen in 16/426 patients (4%)

At 1 year post-diagnosis, low rate of resolution of:

- **serum cryptococcal antigen positivity (25% resolved)**
- **lung imaging abnormalities (34% resolved)**

26% d'infection à *C. Gattii*:

- Plus souvent immunocompétents (73% vs 27%)
- Atteinte neuro-méningée plus fréquente (78% vs 47%)

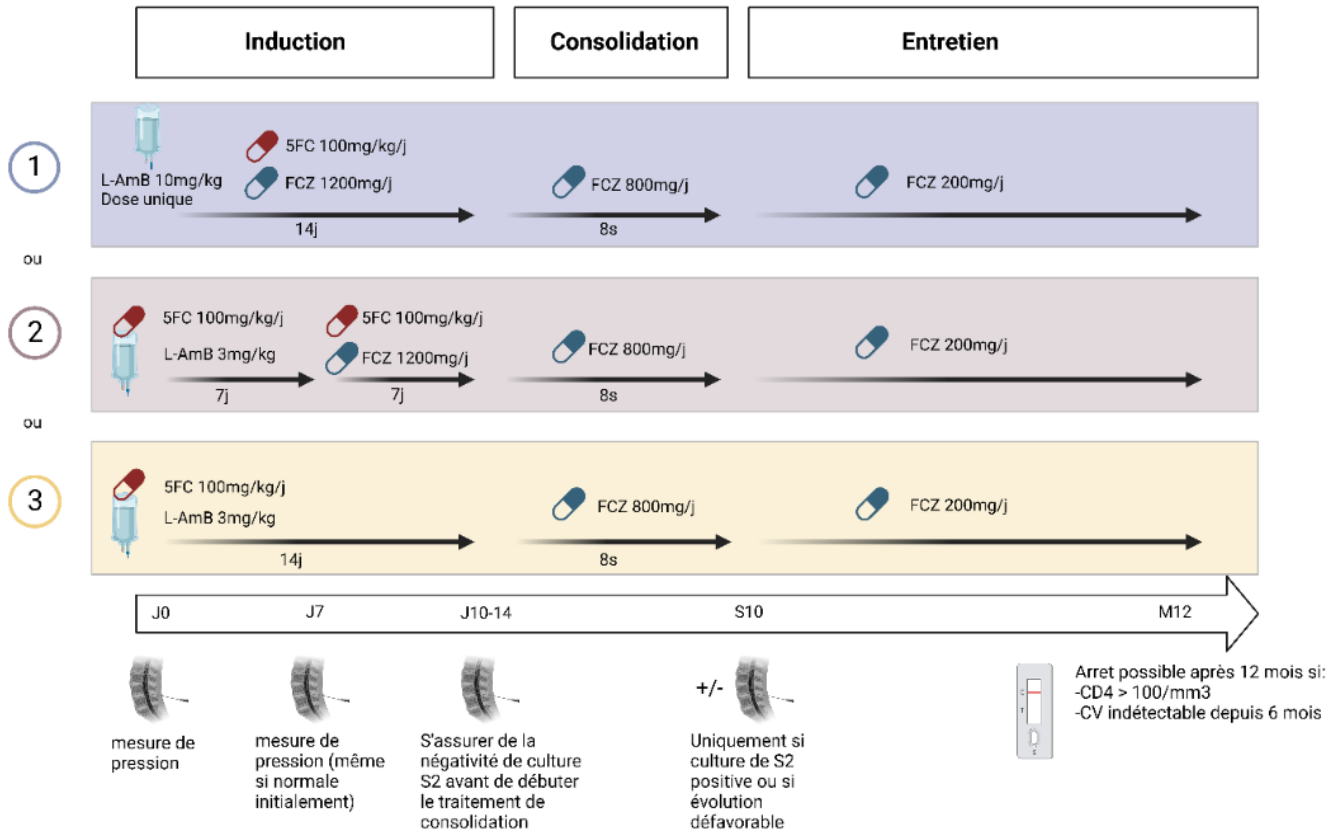
Mortalité à 1 an : 21%

Coussement *et al.*, CID, 2024

Rapport Delobel 2024

- Prise en charge des complications infectieuses associées à l'infection par le VIH
  → Fiche synthétique
  → Recommandations de prise en charge
  → Argumentaire de prise en charge

Recommandations thérapeutiques pour la cryptococcose neuroméningé chez les PVVIH



- Bilan d'extension : PL, hémoculture, culture d'urine (chez l'homme), TDM thoracique et IRM cérébrale en cas de méningite

- Traitement pré-emptif d'un Ag cryptocoque chez un PvVIH asymptomatique : fluconazole 1200 mg/j pendant 2 semaines puis consolidation et traitement d'entretien

- Arrêt de la prophylaxie secondaire > 1an, si CD4>100/mm3 et CV indétectable > 6mois

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] Enock Kagimu,[1] 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] David B. Meya,[1,3,7] and Lillian Tugume[1]

Efficacité du protocole d'induction AMBITION pour le traitement de la cryptococcose neuroméningée chez les PvVIH en vie réelle ?

- Application des recommandations OMS 2022 : L-AmB 10 mg/kg J1 puis fluconazole 1200 mg/j + 5FC 100 mg/kg/j - 14 jours

- Cohorte observationnelle : 179 adultes en Ouganda (comparés aux patients de l'essai AMBITION)

	AMBITION	cohorte
PL	J1, J7, J14	J1, J3 +/- selon évolution
Iono, créat	J1, J3, J5, J7, J10, J12, J14, J28	décision médecin
NFS, BHC	J1, J7, J14, J28	décision médecin
hospit	7 jours minimum	5 jours minimum
suivi	/2 semaines	Selon évolution

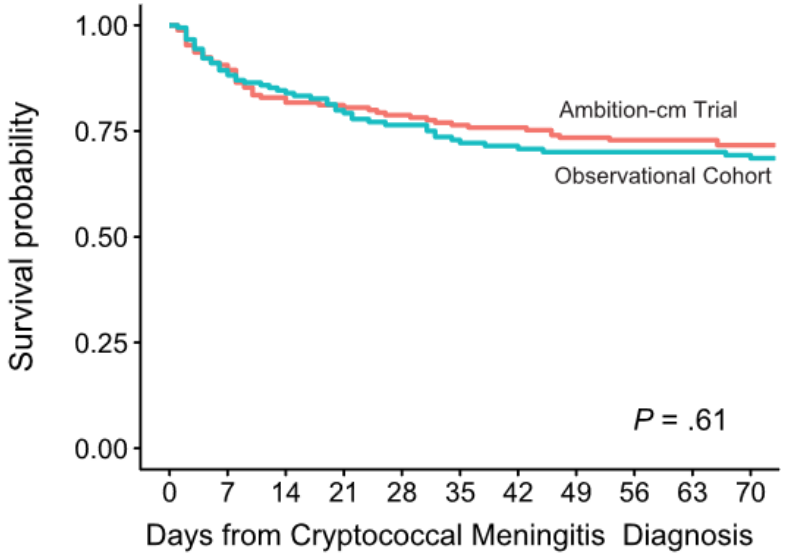
→ 2 en médiane

→ 50% au moins 1 prise de sang de suivi

→ 11 jours en médiane

→ 19% de perdus de vue
3% ré-hospit pour HTIC

Gakuru *et al.*, CID, 2024



Mortalité à S2 :16%
vs 40% (cohortes historiques 2017-2019)

Implémentation du dépistage par Ag crypto

Merci pour votre attention !