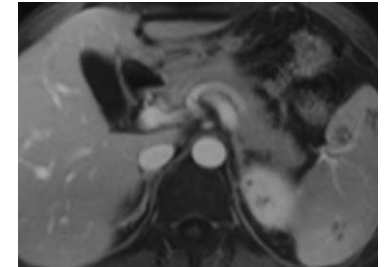
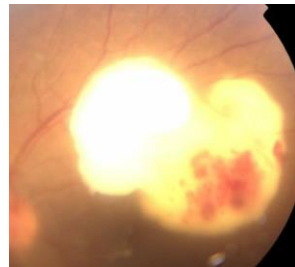


08/10/2024

30^{ème} JRPI Lille Session Recommandations

Recommandation candidose et candidémie



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Déclaration de liens d'intérêt avec les industries de santé en rapport avec le thème de la présentation (loi du 04/03/2002) :

Date : 08/10/2024

Titre : Recommandations européennes candidoses

- | | | | |
|--|--|---|---|
|  | Consultant ou membre d'un conseil scientifique (Takeda) | ☒ OUI | ☐ NON |
|  | Conférencier ou auteur/rédacteur rémunéré d'articles ou documents | ☐ OUI | ☒ NON |
|  | Prise en charge de frais de voyage, d'hébergement ou d'inscription à des congrès ou autres manifestations (Gilead, Takeda, Grifolds) | ☒ OUI | ☐ NON |
|  | Investigateur principal d'une recherche ou d'une étude clinique | ☐ OUI | ☒ NON |

DPI en ligne sur infectiologie.com

Global Guideline for the Diagnosis and Management of Candidiasis:

An Initiative of the ECMM in Cooperation with ISHAM



ESCMID* guideline for the diagnosis and management of *Candida* diseases 2012: non-neutropenic adult patients

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Global Guideline for the Diagnosis and Management of Candidiasis:

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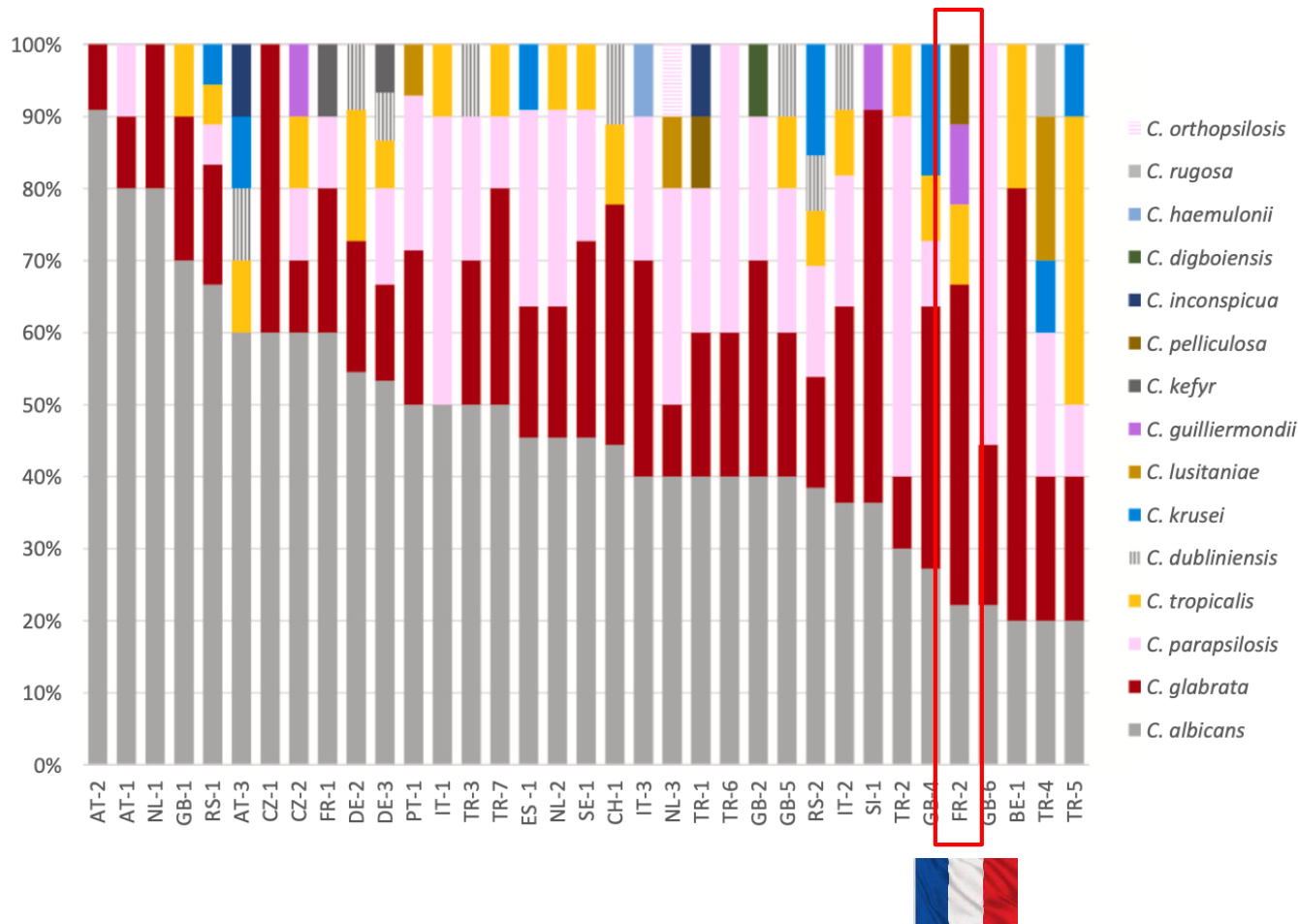


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J. ²⁸, ²⁹, ³⁰, ³¹, ³², ³³, ³⁴, ³⁵, ³⁶, ³⁷, ³⁸, ³⁹, ⁴⁰, ⁴¹, ⁴², ⁴³, ⁴⁴, ⁴⁵, ⁴⁶, ⁴⁷, ⁴⁸, ⁴⁹, ⁵⁰, ⁵¹, ⁵², ⁵³, ⁵⁴, ⁵⁵, ⁵⁶, ⁵⁷, ⁵⁸, ⁵⁹, ⁶⁰, ⁶¹, ⁶², ⁶³, ⁶⁴, ⁶⁵, ⁶⁶, ⁶⁷, ⁶⁸, ⁶⁹, ⁷⁰, ⁷¹, ⁷², ⁷³, ⁷⁴, ⁷⁵, ⁷⁶, ⁷⁷, ⁷⁸, ⁷⁹, ⁸⁰, ⁸¹, ⁸², ⁸³, ⁸⁴, ⁸⁵, ⁸⁶, ⁸⁷, ⁸⁸, ⁸⁹, ⁹⁰, ⁹¹, ⁹², ⁹³, ⁹⁴, ⁹⁵, ⁹⁶, ⁹⁷, ⁹⁸, ⁹⁹, ¹⁰⁰, ¹⁰¹, ¹⁰², ¹⁰³, ¹⁰⁴, ¹⁰⁵, ¹⁰⁶, ¹⁰⁷, ¹⁰⁸, ¹⁰⁹, ¹¹⁰, ¹¹¹, ¹¹², ¹¹³, ¹¹⁴, ¹¹⁵, ¹¹⁶, ¹¹⁷, ¹¹⁸, ¹¹⁹, ¹²⁰, ¹²¹, ¹²², ¹²³, ¹²⁴, ¹²⁵, ¹²⁶, ¹²⁷, ¹²⁸, ¹²⁹, ¹³⁰, ¹³¹, ¹³², ¹³³, ¹³⁴, ¹³⁵, ¹³⁶, ¹³⁷, ¹³⁸, ¹³⁹, ¹⁴⁰, ¹⁴¹, ¹⁴², ¹⁴³, ¹⁴⁴, ¹⁴⁵, ¹⁴⁶, ¹⁴⁷, ¹⁴⁸, ¹⁴⁹, ¹⁵⁰, ¹⁵¹, ¹⁵², ¹⁵³, ¹⁵⁴, ¹⁵⁵, ¹⁵⁶, ¹⁵⁷, ¹⁵⁸, ¹⁵⁹, ¹⁶⁰, ¹⁶¹, ¹⁶², ¹⁶³, ¹⁶⁴, ¹⁶⁵, ¹⁶⁶, ¹⁶⁷, ¹⁶⁸, ¹⁶⁹, ¹⁷⁰, ¹⁷¹, ¹⁷², ¹⁷³, ¹⁷⁴, ¹⁷⁵, ¹⁷⁶, ¹⁷⁷, ¹⁷⁸, ¹⁷⁹, ¹⁸⁰, ¹⁸¹, ¹⁸², ¹⁸³, ¹⁸⁴, ¹⁸⁵, ¹⁸⁶, ¹⁸⁷, ¹⁸⁸, ¹⁸⁹, ¹⁹⁰, ¹⁹¹, ¹⁹², ¹⁹³, ¹⁹⁴, ¹⁹⁵, ¹⁹⁶, ¹⁹⁷, ¹⁹⁸, ¹⁹⁹, ²⁰⁰, ²⁰¹, ²⁰², ²⁰³, ²⁰⁴, ²⁰⁵, ²⁰⁶, ²⁰⁷, ²⁰⁸, ²⁰⁹, ²¹⁰, ²¹¹, ²¹², ²¹³, ²¹⁴, ²¹⁵, ²¹⁶, ²¹⁷, ²¹⁸, ²¹⁹, ²²⁰, ²²¹, ²²², ²²³, ²²⁴, ²²⁵, ²²⁶, ²²⁷, ²²⁸, ²²⁹, ²³⁰, ²³¹, ²³², ²³³, ²³⁴, ²³⁵, ²³⁶, ²³⁷, ²³⁸, ²³⁹, ²⁴⁰, ²⁴¹, 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Epidémiologie - ↗ *Candida non albicans*

European candidaemia is characterised by notable differential epidemiology and susceptibility pattern: Results from the ECMM *Candida* III study

Maiken Cavling Arendrup [Journal of Infection 87 \(2023\) 428–437](#)



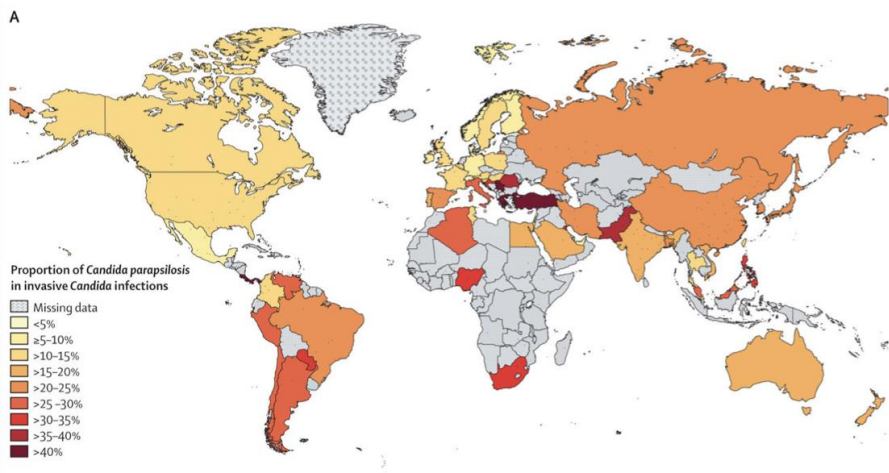
→ **Concept**
« Difficult to treat
non albicans species »

Epidémiologie - *Candida parapsilosis* FlucoR

Worldwide emergence of fluconazole-resistant *Candida parapsilosis*: current framework and future research roadmap

Farnaz Daneshnia*,

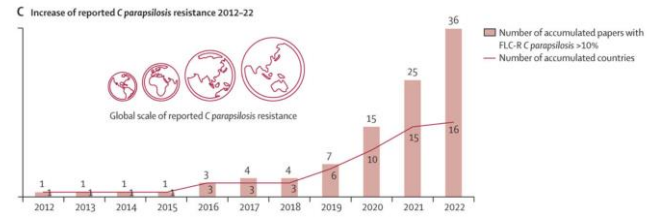
3^{ème} espèce mondiale candidémies



Epidémiologie - *Candida parapsilosis* FlucoR

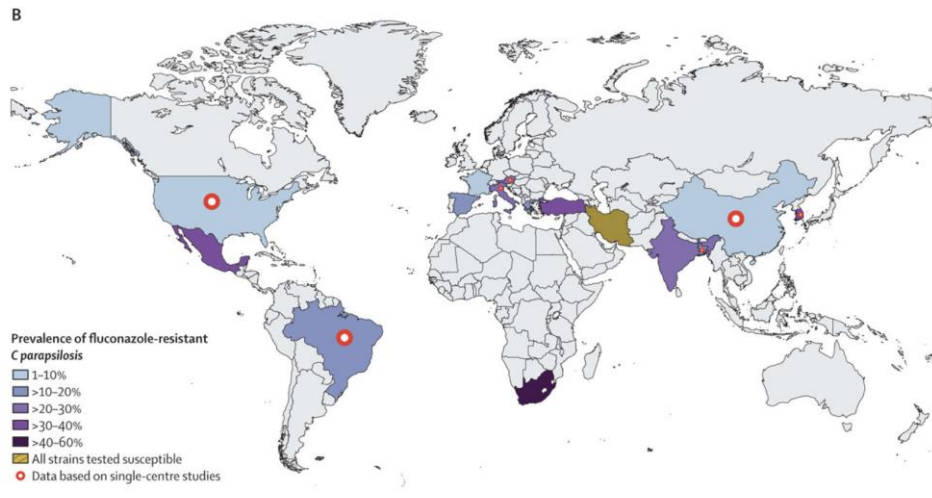
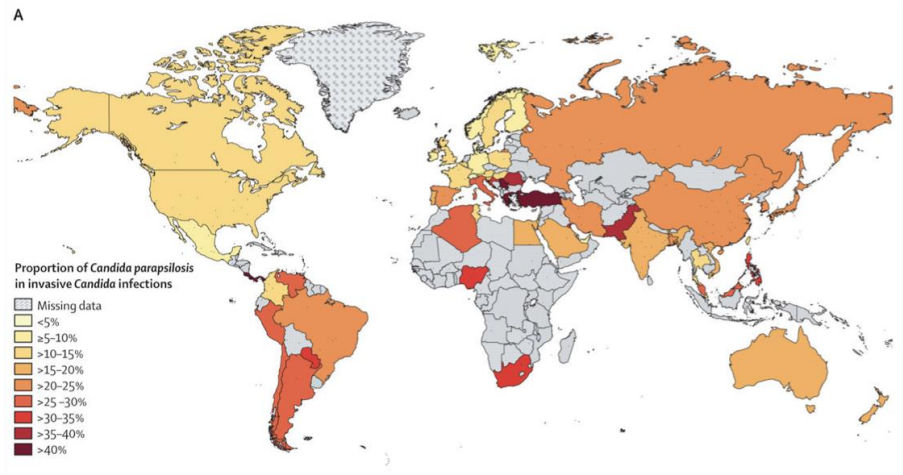
Worldwide emergence of fluconazole-resistant *Candida parapsilosis*: current framework and future research roadmap

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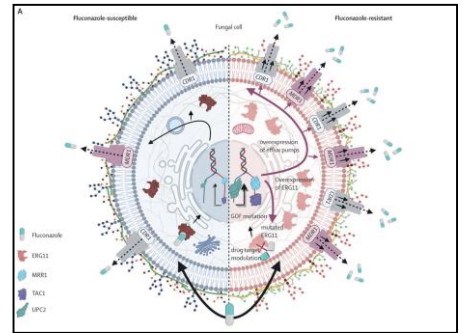


3^{ème} espèce mondiale candidémies

Candines R + azolés R



- Fekkar AAC 2021, Presente AAC 2023
- Jusque ≈ 10% souches
 - Emergent sous fluconazole
 - Substitution gène ERG → persistance et diffusion
 - Transmission nosocomiale, clusters

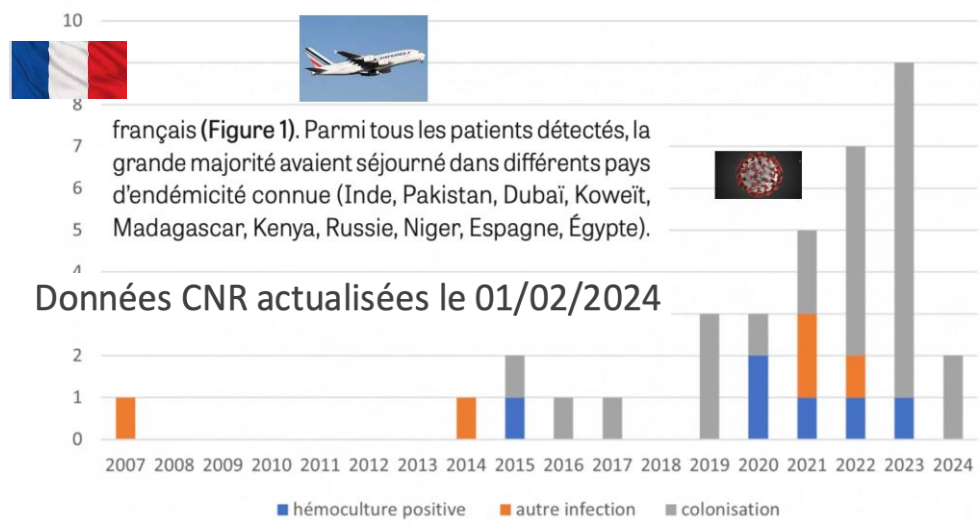
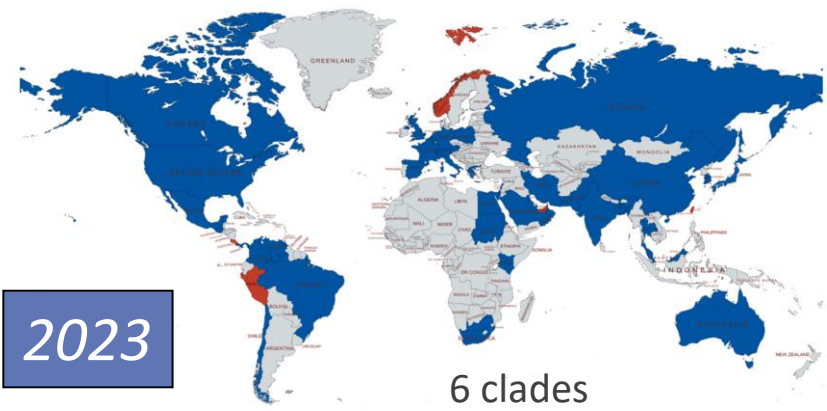


Epidémiologie - *Candida auris*

Candida auris: A bibliometric analysis of an emerging global health threat

+ *Candida haemulonii*

Journal of Infection and Public Health 16 (2023) Paolo Ragusa



→ Table 3. Infection control recommendations for prevention of invasive candidiasis.

Taxonomie



<i>C. glablatra</i>	→	<i>Nakaseomyces glablatra</i>
<i>C. guilliermondii</i>	→	<i>Meyerozyma guilliermondii</i>
<i>C. lusitaniae</i>	→	<i>Clavispora lusitaniae</i>
<i>C. krusei</i>	→	<i>Pichia kudriavzevii</i>
<i>C. rugosa</i>	→	<i>Diutina rugosa</i>

Diagnostic



- **Apport de la TEP**

<i>Candida</i> endocarditis	To diagnose	Echocardiography, [18F]- FDG PET/CT	A	Ilu	Fernandez-Cruz EJCMJ 2015 ²⁷⁵	TTE pos. (2.9%) vs TEE pos. (11.5%)
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- **T2MR *Candida*** = nanoparticule couplée à PCR - limites +++

Recommendation – Currently, no molecular technique is strongly recommended for any patient population in diagnosing IC, as pathogen detection is restricted to a limited number of species, and its position in routine clinical use is unclear. As commercial assays (e.g., T2 *Candida*) will have undergone more extensive analytical and clinical validation their use is preferred over in-house methods lacking supporting validation. The use of

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- **13BDG :**

- recommandé pour le diagnostic
- ne pas initier d'AF sur des 13BDG+ isolés

It is strongly recommended that all serological markers for candidaemia/IC must only be used in conjunction with clinical parameters, other biomarkers and or other diagnostic tools.

- faible valeur pour arrêt d'un traitement préemptif
- intérêt dans le LCS

Traitement - candidémie



Candidemia without organ involvement

Consider local epidemiology and review treatment decision in light of susceptibility testing results

First-line treatment – If all options available

Anidulafungin* 200 mg qd d1; 100 mg qd from d2	Caspofungin* 70 mg qd d1; 50 mg qd from d2	Micafungin* 100 mg qd	Rezafungin 400 mg qw; 200 mg qw from w2	Fluconazole* 400 mg qd or bid	Voriconazole* 6 mg/kg bid d1; 4 mg/kg bid from d2	Liposomal amphotericin B* 3 mg/kg qd	Amphotericin B lipid complex* 5 mg/kg qd	Isavuconazole* 200 mg tid d1-2; 200 mg qd from d3	Deoxycholate amphotericin B* any dose	Itraconazole* 200-400 mg qd
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Rezafungin versus caspofungin for treatment of candidaemia and invasive candidiasis (ReSTORE): a multicentre, double-blind, double-dummy, randomised phase 3 trial

Lancet 2023; 401: 49–59

George R Thompson III, Alex Soriano, Oliver A Cornely, Bart Jan Kullberg, Marin Kollef, Jose Vazquez, Patrick M Honore, Matteo Bassetti, John Pullman, Methee Chayakulkeeree, Ivan Poromanski, Cecilia Dignani, Anita F Das, Taylor Sandison, Peter G Pappas, on behalf of the ReSTORE trial investigators

Strongly recommended
Moderately recommended
Marginally recommended
Recommended against



Traitement - candidémie



Candidemia without organ involvement

Consider local epidemiology and review treatment decision in light of susceptibility testing results

First-line treatment – If all options available

Anidulafungin* 200 mg qd d1; 100 mg qd from d2	Caspofungin* 70 mg qd d1; 50 mg qd from d2	Micafungin* 100 mg qd	Rezafungin 400 mg qw; 200 mg qw from w2	Fluconazole* 400 mg qd or bid	Voriconazole* 6 mg/kg bid d1; 4 mg/kg bid from d2	Liposomal amphotericin B* 3 mg/kg qd	Amphotericin B lipid complex* 5 mg/kg qd	Isavuconazole* 200 mg tid d1-2; 200 mg qd from d3	Deoxycholate amphotericin B* any dose	Itraconazole* 200-400 mg qd
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CVC removal

as early as possible (<48-72h) if in place

Daily follow-up blood cultures until 3 consecutive negative days

If blood from d5 is positive, repeat search for intravascular or other uncontrolled source

Strongly recommended
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Traitement - candidémie



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CVC removal

as early as possible (<48-72h) if in place

Daily follow-up blood cultures until 3 consecutive negative days

If blood from d5 is positive, repeat search for intravascular or other uncontrolled source

*After 5 days of 1st line treatment consider switch to oral, if all 6 pre-requisites fulfilled:

1. Haemodynamically stable
2. Documented clearance of *Candida* from blood stream
3. Non-neutropenic
4. Source control
5. Oral azole tolerated
6. Susceptibility confirmed

If blood cultures from day five are still positive, repeat search for an intravascular, or other uncontrolled source

Durée de traitement = 14 jours

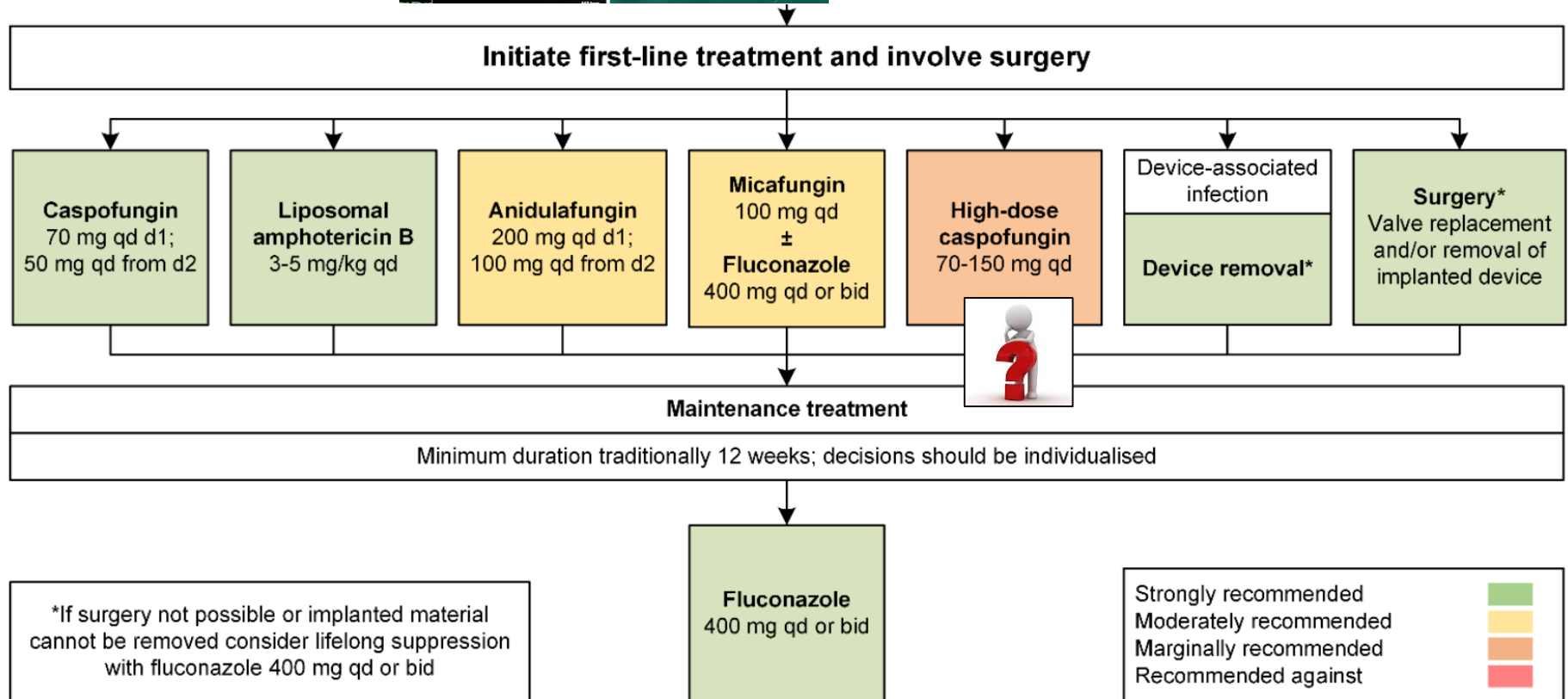
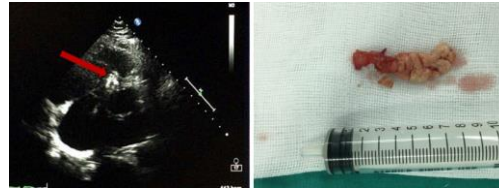
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Traitement



- Endocardite

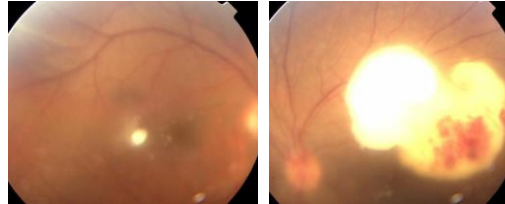


The guideline strongly recommends a duration of therapy of at least 6 weeks after surgery and longer if there are complications, in particular paravalvular abscess. Longer courses are required when surgery is not possible.

Traitement



- Endocardite
- Endophtalmie



Endophthalmitis

Overall traditional treatment duration 4-6 weeks; decisions should be individualised

Fluconazole
100 mg qd-bid

**Liposomal
amphotericin B**
3 mg/kg qd

Voriconazole
6 mg/kg bid d1;
4 mg/kg bid from d2

**Intravitreal
deoxycholate
amphotericin B**
with variable
duration/doses

Discuss early vitrectomy

Strongly recommended
Moderately recommended
Marginally recommended
Recommended against



Traitement - dosage AF



- Dosage des azolés et candines si disponible chez :
 - NN prématurés
 - patients de réa avec volume de distribution modifié
 - circuits extra-corporels
 - hypoalbuminémie
 - interactions prévisibles
 - malabsorption
 - obèse

➤ Front Pharmacol. 2022 Nov 3;13:993330. doi: 10.3389/fphar.2022.993330. eCollection 2022.

The recommended dosage regimen for caspofungin in patients with higher body weight or hypoalbuminaemia will result in low exposure: Five years of data based on a population pharmacokinetic model and Monte–Carlo simulations

Qianting Yang¹, Tao Zhang², Ying Zhang², Dan Sun^{2,3}, Xiaowei Zheng^{3,4}, Qian Du²,
Xue Wang^{4,5}, Xiaoliang Cheng², Jianfeng Xing^{5,6}, Yalin Dong²

Réa, prescription en mg/kg

Prélevé le 15/09/23 à 07:13		Enregistré le 15/09/23 à 07:24		Édité le 28/09/23 à 11:41		Complet	
Rens. clinique : prélèvement sur brycker							
TOXICOLOGIE							
Médecin / Service		Pr Arnaud Villers					
Posologie journalière		70					
Mode d'administration		Non communiquée					
Date et heure dernière dose		14/9/2023 14h00					
Date et heure de Prélèvement		15/9/2023 7h00					
Motif de la prescription		Suivi					
Traitement associé		Non communiqué					
Dosage plasmatique des antifongiques							
Caspofungine (LC-MS/MS)		1.9		mg/L		(COM)	
Les concentrations plasmatiques résiduelles et en pic (T_{1h}) après administration de 50 mg/jour de caspofungine sont respectivement de l'ordre de 1,8 mg/L et 10 mg/L. La caspofungine présente une pharmacocinétique non-linéaire (élimination tri-phasique) avec risque d'accumulation accrue lorsque la dose croît, cette molécule n'étant par ailleurs pas dialysable. Elle présente une liaison forte à l'albumine (55 à 97%) et une faible excrétion rénale de la molécule mère (2%). Source : Vidal							
Analyse/Interprétation des résultats : Concentration en caspofungine de l'ordre des concentrations attendues en résiduel.							
(COM)							

Traitement - intérêt de l'infectiologue/stewardship AF

- Amélioration de la prise en charge :
 - rapidité de ttt
 - plus d'ablation de KT
 - plus d'échographie cardiaque et de FO



Recommendation – Based on the existing evidence, the guideline group recommends including AFS as an essential component in AMS programs and quality improvement management. When implementing AFS, structures should be tailored to international recommendations. In addition, we advocate for the establishment of national or international excellence centres that can provide professional advice.

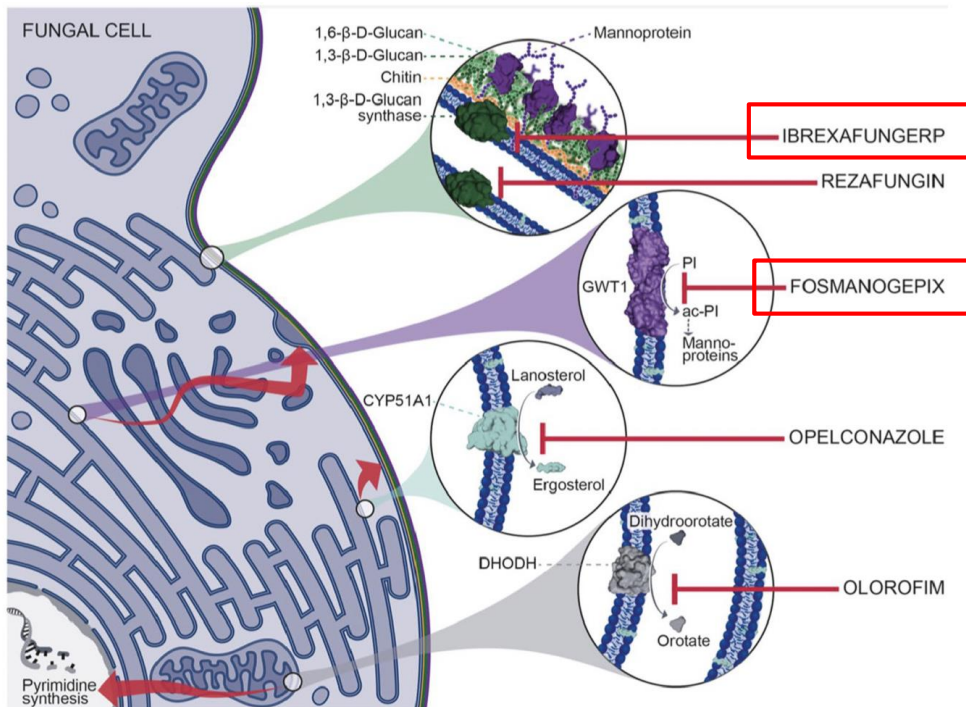
- Promotions d'outils de bon usage locaux



Conclusion



- Questions non résolues
 - applicabilité recommandations high/low resource countries
 - outils dg simple comportant *C. auris*
 - durée de ttt, place des bithérapies
 - place des nouveaux antifongiques

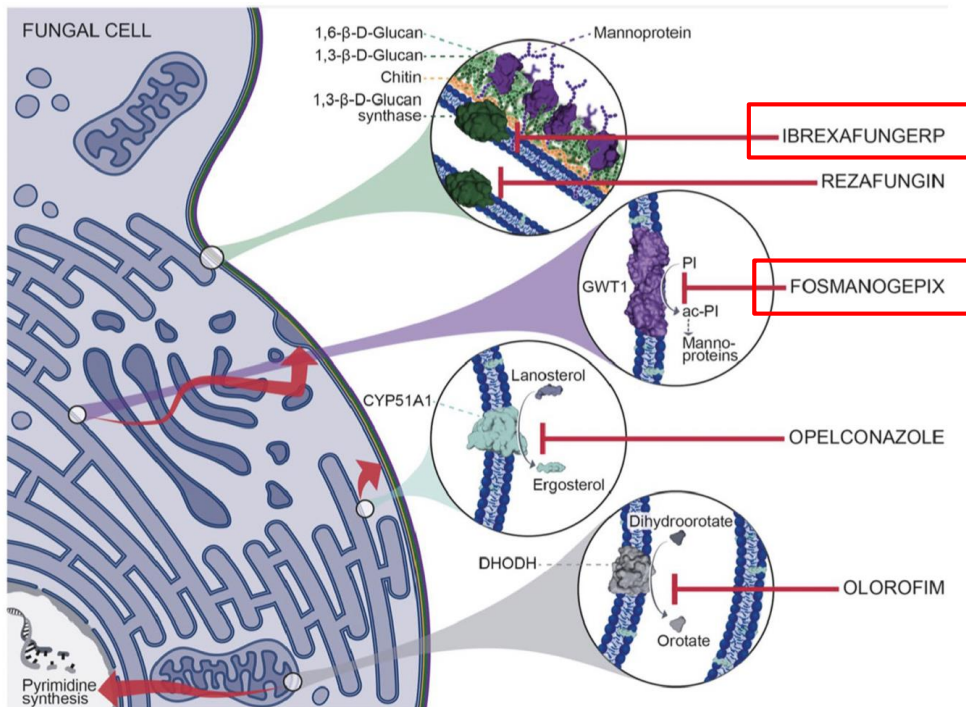


Adapted from Hoeniglet al, 2022

Conclusion



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Adapted from Hoeniglet al, 2022

Merci