SCUOLA DI SPECIALIZZAZIONE IN MALATTIE INFETTIVE E TROPICALI

PANDORA ID - 24

TIME TO WEBINAR IN INFECTIOUS DISEASES

# ESCMID Global/ECCMID: Novità in Tema di Infezioni Fungine

Dott. Giacomo Casalini
ASST Fatebenefratelli Sacco
S.C. Malattie Infettive III

26.09.2024

# Disclosures

I declare no competing interests.

# ESCMID Global and Fungal Infections

**EPIDEMIOLOGY, OUTBREAKS AND CLIMATE CHANGE**

**DIAGNOSTIC TECNIQUES AND STRATEGIES**

**ANTIFUNGAL RESISTANCE AND TREATMENT**

# Epidemiology

## Global incidence and mortality of severe fungal disease

David W Denning

6.55 mln cases

3.75 mln deaths

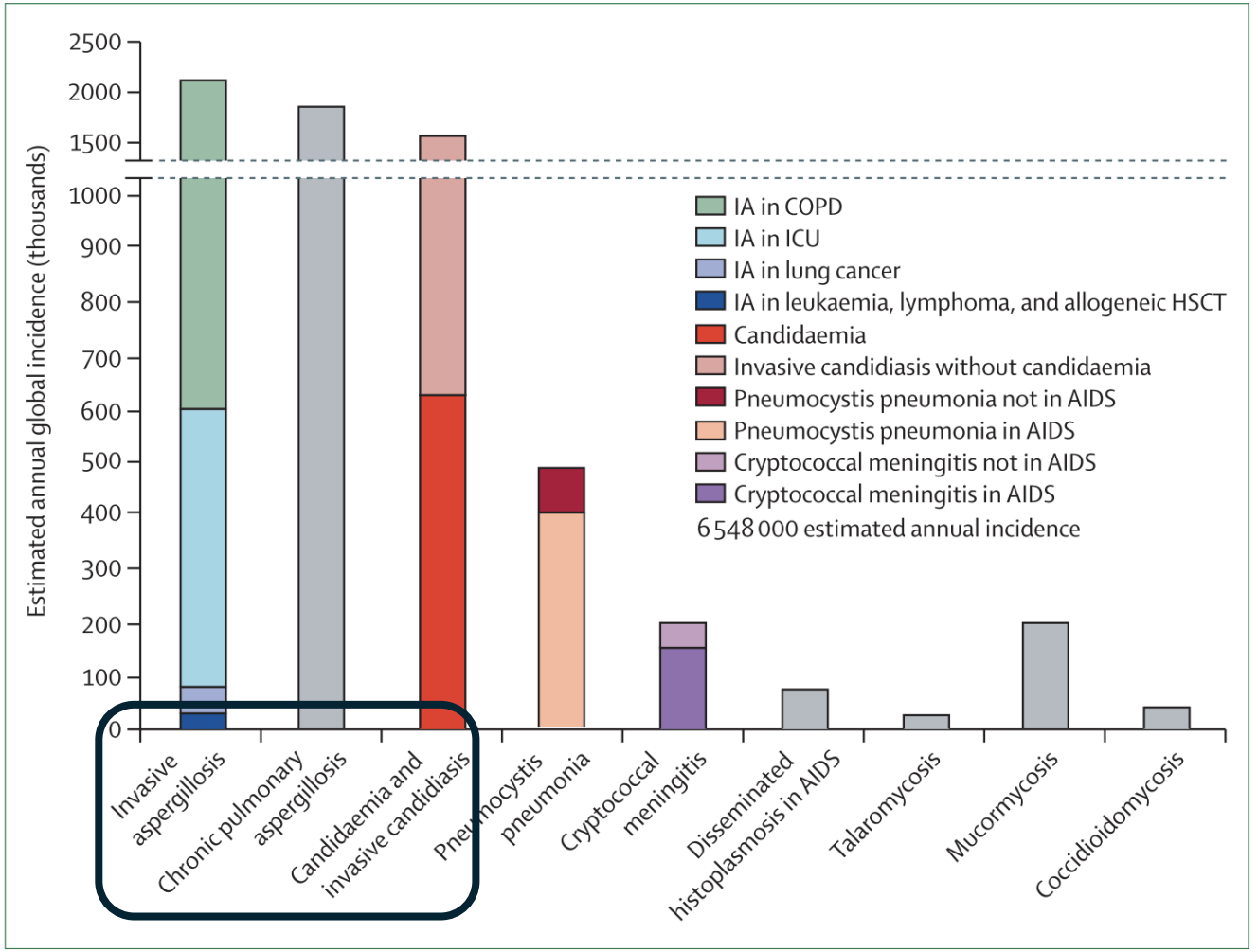


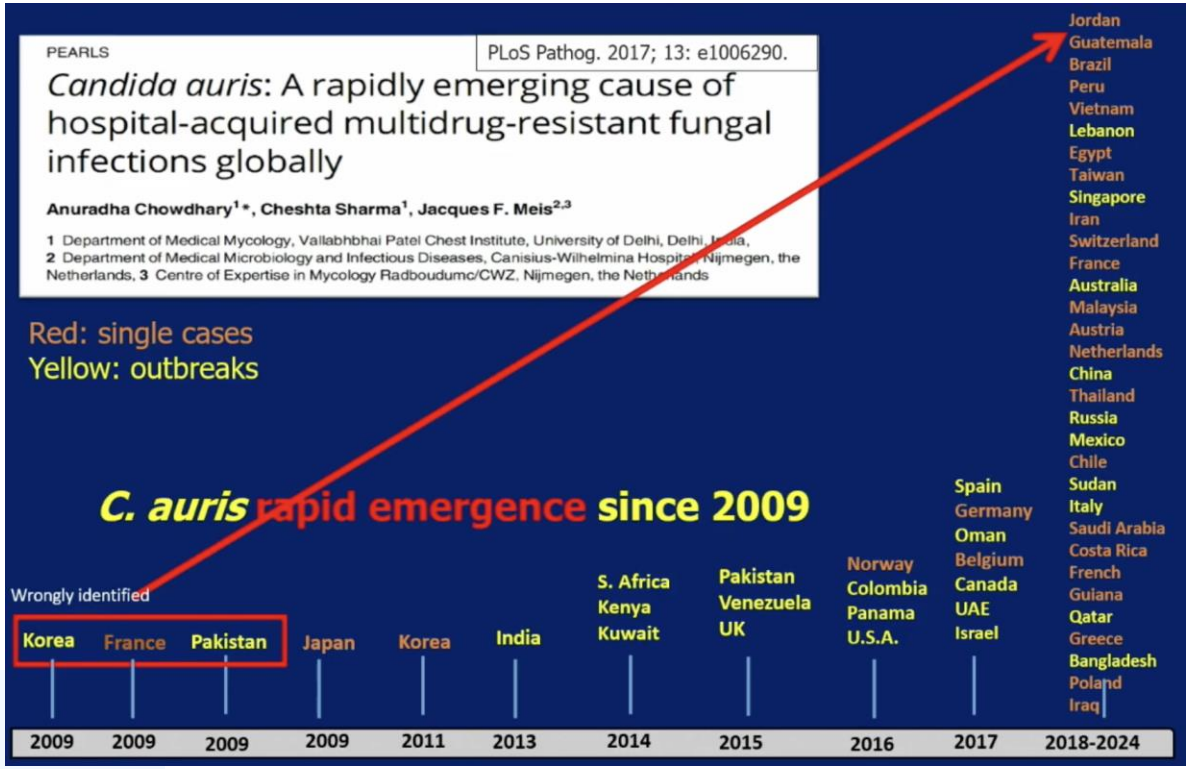

*Figure 1:* **Estimated annual incidence of life-threatening invasive mycoses, together with chronic pulmonary aspergillosis**

# Epidemiology - *Candida auris*

Highly divergent genome from yeasts in the CTG clade

Clades: I-IV global spread, V Iran + VI (Bangladesh/Singapore)

Italy: 2019, clade I (South Asia), Genova




**E1035**

**Discovery of the sixth *Candida auris* clade: molecular epidemiology in Singapore**

06. Fungal infection & disease
06a. Fungal disease epidemiology

K.K.K. Ko [1], C.S. Suphavilai [2], K.M. Lim [2], M.G. Tan [1], B. Patipan [2], J.J.K. Chu [2], W.E. Ong [1], J.H.C. Sim [3], Y.E. Tan [1], J.F. Meis [4], C.K.M. Tsui [5], N. Nagarajan [2].

*[1]Singapore General Hospital - Singapore (Singapore), [2]Genome Institute of Singapore - Singapore (Singapore), [3]Parkway Laboratory Services Pte Ltd - Singapore (Singapore), [4]Center of Expertise in Mycology Radboud University Medical Center - Nijmegen (Netherlands), [5]National Centre for Infectious Diseases - Singapore (Singapore)*

# Why *C. auris* is a threat

01

**Persistance**

Colonization of multiple body sites (skin) and hospital environment

02

**Resistance**

Multifactorial and variable antifungal resistance

03

**Spread**

**S**ignificant risk of nosocomial outbreaks requiring strong IPC efforts

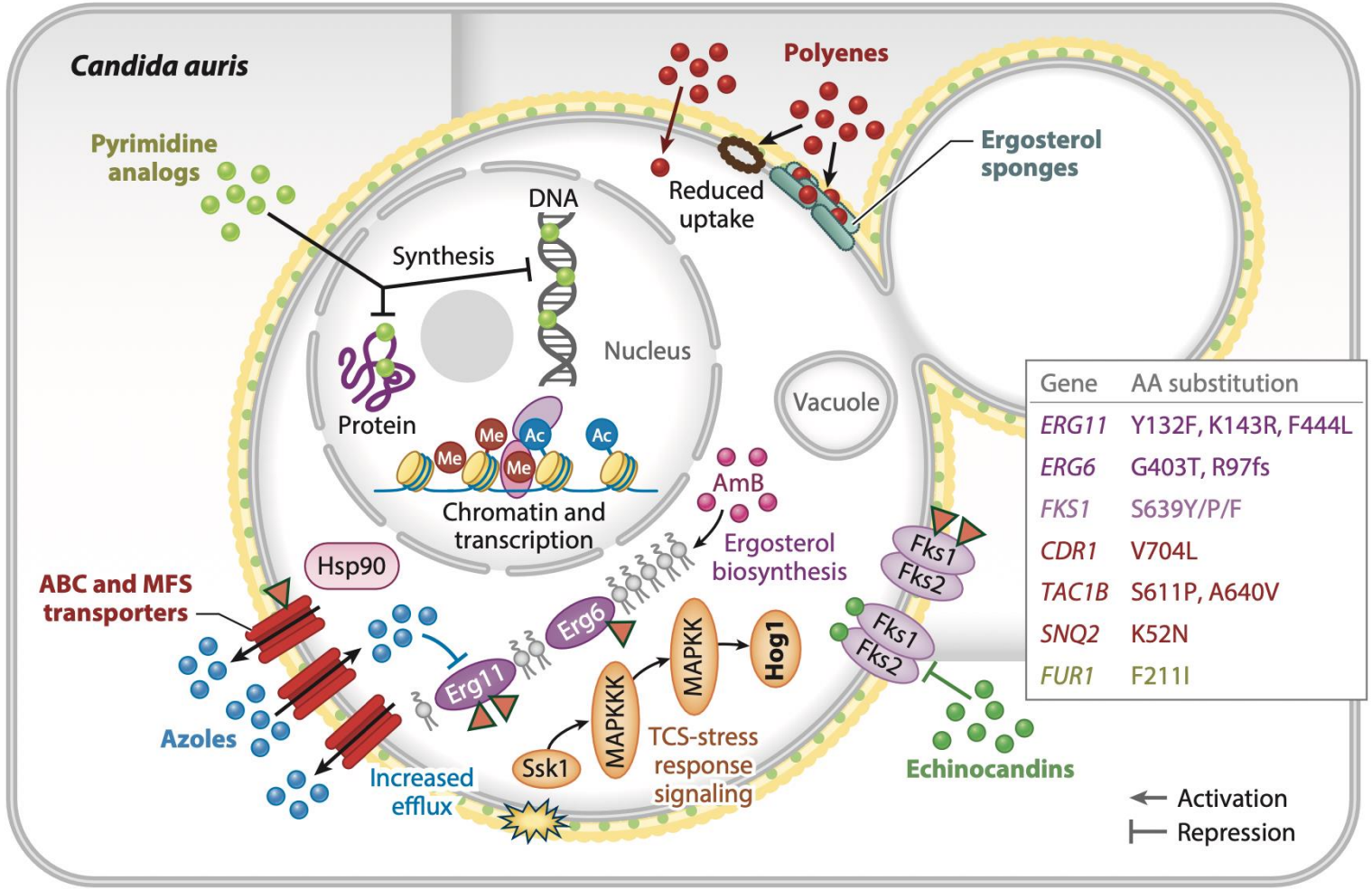
04

**Mortality**

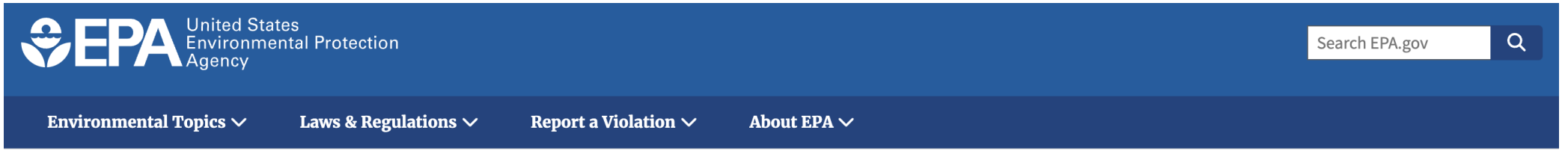
Pooled crude mortality of 41% [95% CI 37-45%] if invasive infection

*Ann Rev Microbiol* 2023; 77: 583-602.

# Antifungal resistance in *C. auris*



# IPC for *Candida auris*




## EPA's Registered Antimicrobial Products Effective Against Candida auris [List P]

Accumulating data indicate that products solely dependent on quaternary ammonia compounds (QACs) are **NOT** effective.

| Country | IPC guidelines |
|---|---|
| UK | UKHSA. *Candida auris*: laboratory investigation, management and infection prevention and control: UK Health Security Agency; 2024[1] |
| USA | CDC. CDC. Infection Prevention and Control for *Candida auris*: Centers for Disease Prevention and Control 2021[2] |
| Europe | ECDC. *Candida auris* in healthcare settings: European Centre for Disease Prevention and Control; 2016[3] |
| South Africa | COTHI. Interim guidance for management of *Candida auris* infections in South African hospitals: Centre for Opportunistic, Tropical and Hospital Infections; 2016[4] |
| South Africa | Federation of Infectious Diseases Societies of Southern Africa guideline: Recommendations for the detection, management and prevention of healthcare-associated *Candida auris* colonisation and disease in South Africa[7] |
| Australia | Diagnosis, management and prevention of *Candida auris* in hospitals: position statement of the Australasian Society for Infectious Diseases. Intern Med J. 2019;49(10):1229-43[5] |
| WHO | PAHO. Epidemiological Alert: Candida auris outbreaks in health care services in the context of the COVID-19 pandemic: Pan American Health Organisation (PAHO); 2021[6] |
| Canada | PHO. Provincial Infectious Diseases Advisory Committee Interim Guide for Infection Prevention and Control of Candida auris 2019[8] |
| Switzerland | Candida auris - recommendations on infection prevention and control measures in Switzerland.[9] |

| High-level disinfectants and/or chemical sterilants | Strength/concentration | Proven Efficacy | Reference |
|---|---|---|---|
| Peracetic acid hydrogen peroxide <1%, acetic acid (OxyCide)<br>Peracetic acid | 1200ppm,<br>0.20% | ≥4.1-log10 reduction | Cadnum et al. 2017<br>Rutala et al.2019 |
| Hydrogen peroxide (Oxivir Tb, Clorox)<br>Hydrogen peroxide plus peroxyacetic acid<br>Accelerated hydrogen peroxide | 0.5%, 1.4%<br>0.65% plus 0.14%<br>2% | ≥4.1-log10 reduction | Cadnum et al. 2017<br>Rutala et al 2019<br>Rutala et al 2019 |
| Vaporized hydrogen peroxide (BioQuell) | 8g/peroxide/$m^3$ | | Abdolrasouli *et al.* 2017 |
| Glutaraldehyde | 2.4% | ≥4.1-log10 reduction | Rutala et al 2019 |
| Ortho-phthalaldehyde | 0.55% | 2.3-log10 reduction | Rutala et al 2019 |
| Ultra violet light | (D90 value of 515 J/m2)<br>Time and distance to exposure | Clades: Venezuela, Spain and India not very susceptible | Schelenz *et al.* unpublished<br>De Groot et al 2019 |

| Low-level disinfectants and other | Strength/concentration | Proven Efficacy | Reference |
|---|---|---|---|
| Sodium hypochloride<br>(Clorox, Chlor-clean, HazTab®) | ≥ 1000 ppm<br>0.39-0.65%, 10% | Some viable strains on stainless steel and polyester coverslips | Cadnum *et al.* 2017<br>Abdolrasouli *et al.* 2017,<br>Moore *et al.* 2017<br>Kean et al., 2018 |
| Quaternary ammonium (Lysol all, Virex II 256) | 0.5% | | Cadnum *et al.* 2017 |
| Ethyl alcohol 29.4% (Purell disinfectant) | 29.4% | | Cadnum *et al.* 2017 |
| Acetic acid (White distilled vinegar) | >5% (pH 2.0) | | Cadnum *et al.* 2017 |

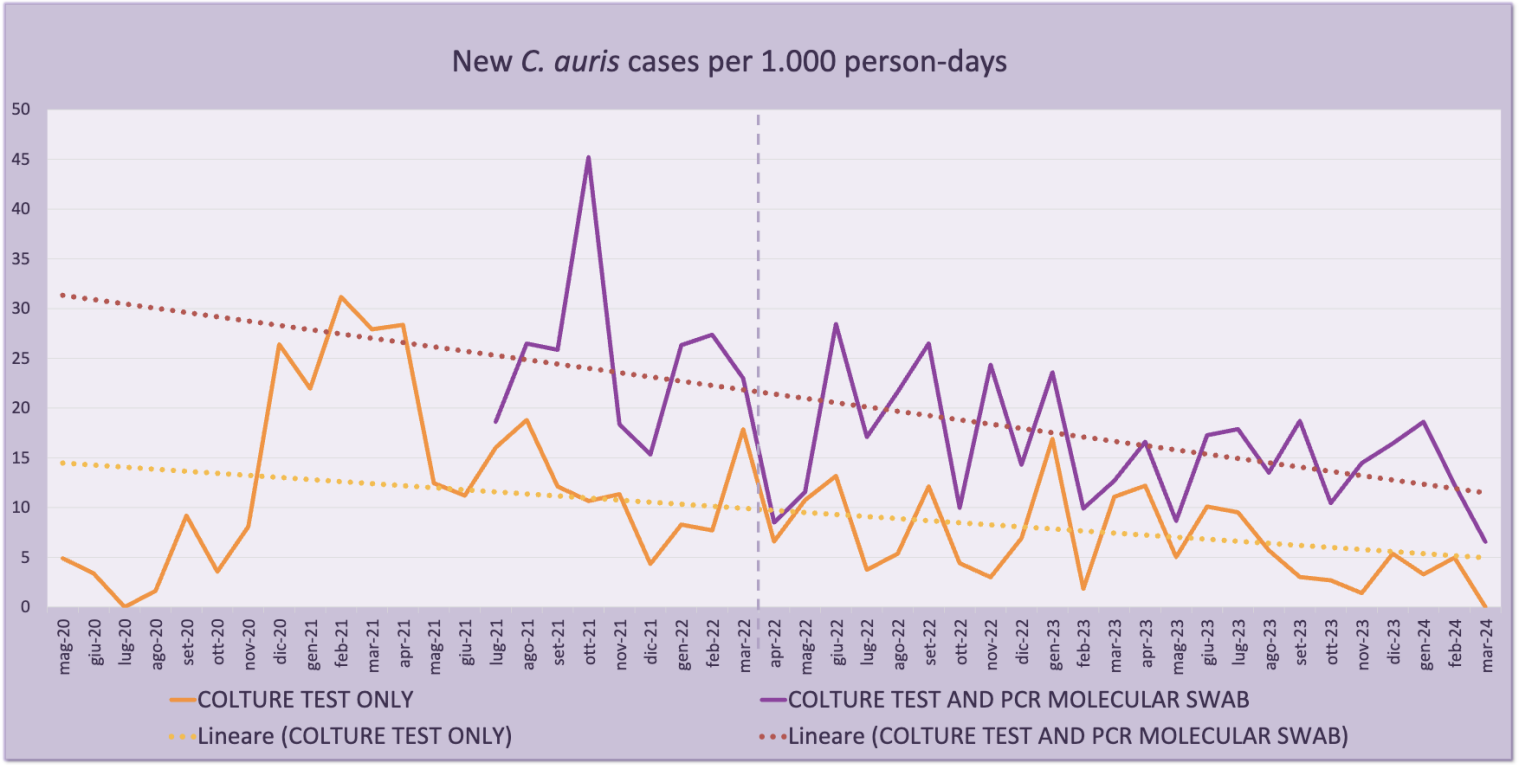
EPA's Registered Antimicrobial Products Effective Against Candida auris [List P] | US EPA

1. mBio. 2023 May-Jun

P2843

# Epidemiologic surveillance of *Candida auris*: a comparative study of pre and post-COVID periods in the ICU at Ospedale Policlinico San Martino IRCCS, Liguria, Italy

L. Massolo[1], E. Baldoni[1], E. Zumerle[1], E. Giribaldi[1], D. Bellina[2], B. Guglielmi[2], M. Paoletti[2], A. Talamini[2], G. Icardi[2,1], A. Orsi[1,2].




Study period: 2021-2023

721 ICU patients screend (12% COVID-19), on admission and weekly

16% colonised; of them, 18% on admission

7% developed candidaemia

P2889

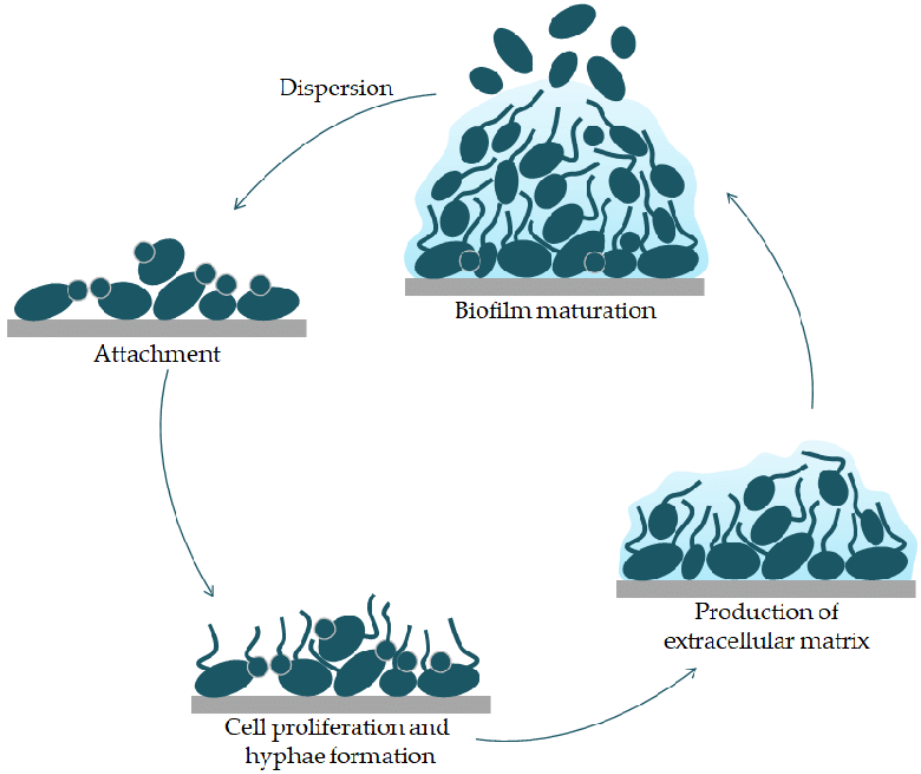
## Screening for *Candida auris* in critically ill patients: a 2-year analysis from a Greek tertiary-care hospital, during COVID-19 waves

V. Mamali[1], N. Rekleiti[1], C. Louka[1], I. Daniil[1], F. Mitropoulou[1], G. Vrioni[2], O. Zarkotou[1]

[1]Department of Microbiology, Tzaneio General Hospital of Piraeus, [2]Department of Microbiology, Medical School, National and Kapodistrian University of Athens

# Epidemiology – *C. parapsilosis*

- Candidaemia in ICU and pre-term neonates
- Echinocandin tolerance
- Fluconazole resistance
- Hospital-based outbreaks

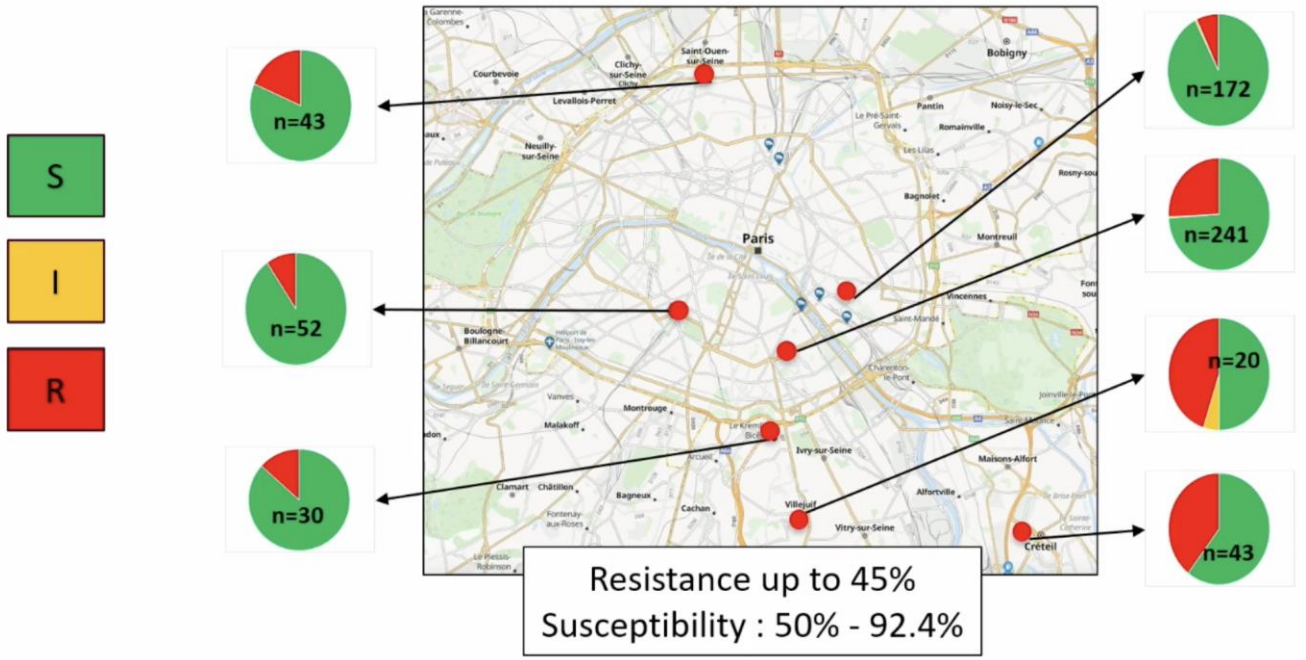



Arendrup MC, et al. J Infect 2023. Chan J, et al. BMC Infect Dis 2020. Ahmad S, et al. Microorganisms 2021. Daneshnia F, et al. Lancet Microbe 2023. Castanheira M, et al. Int J Antimicrob Agents 2020

# ReCaP multi-centre study

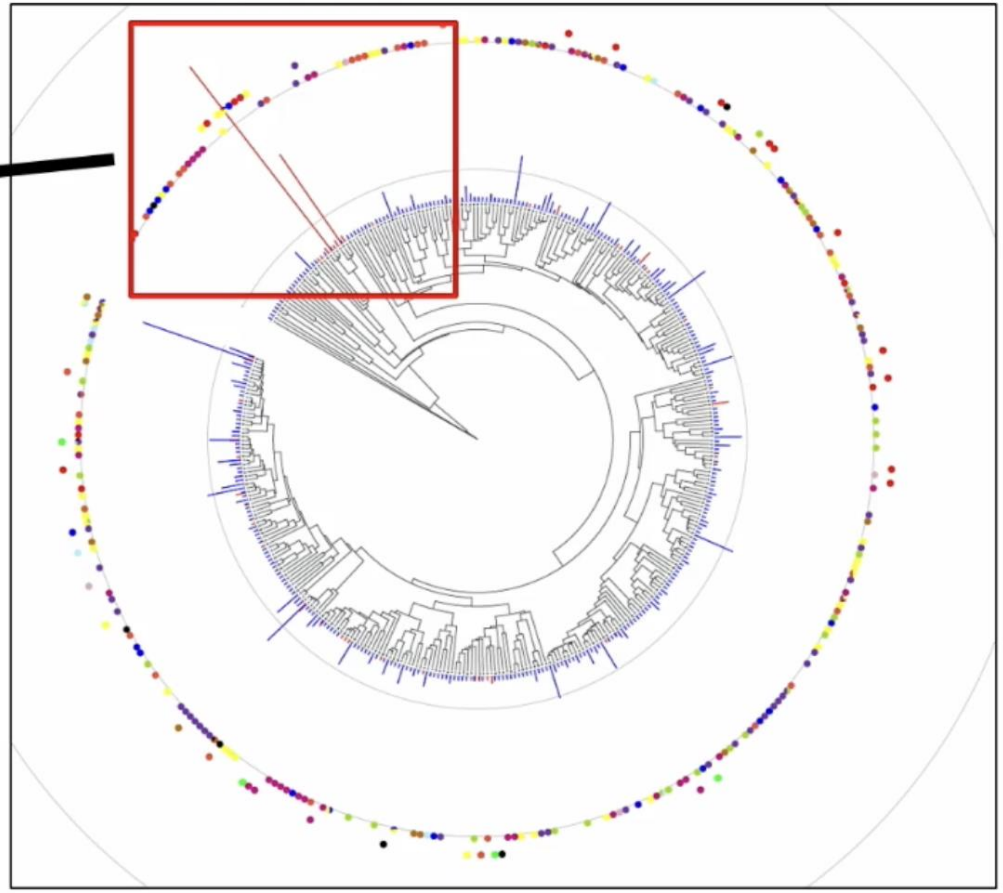
- France, prospective, 16 labs, starting April 2022
- 2620 isolates, 1540n patients
- Fluconazole E-TEST (R se MIC >

**10.6% of patients with resistance strains**



# ReCaP multi-centre study

Circulation of 2 resistant clones in Paris area



Genotyping analysis based on microsatellite length polymorphism for 784 *Candida parapsilosis* isolates collected in 16 french hospitals between April 2022 and September 2023

Original Article

# Genotypic and phenotypic characteristics of *Candida parapsilosis* bloodstream isolates: Health Care Associated Infections in a teaching Hospital in Italy

Giuseppina Caggiano [a,*,1], Simona Fioriti [b,1], Gianluca Morroni [b,1], Francesca Apollonio [a,1], Francesco Triggiano [a], Gloria D'Achille [b], Pasquale Stefanizzi [a], Lidia Dalfino [c], Luigi Ronga [d], Adriana Mosca [e], Eleonora Sparapano [d], Carmela De Carlo [d], Fabio Signorile [f], Salvatore Grasso [c], Francesco Barchiesi [b,g,**], Maria Teresa Montagna [a]

April – October 2022

Clonal dissemination of FLU-R isolates

All isolates were susceptible to amphotericin B and anidulafungin with MICs ranges of 0.06–0.5 and 0.25–1 µg/ml, respectively (Table 1). Only 9/50 isolates (18%) were fluconazole susceptible with MICs range of 0.5–1 µg/ml, the other isolates 41/50 (82 %) were resistant to the antifungal with MICs of 64–128 µg/ml. All Fluconazole-Resistant (FR) strains harbored the amino acid substitution Y132F in the protein ERG11, in addition *C. parapsilosis* n. 19 also harbored D355N. Finally, 5/7 Fluconazole-Susceptible (FS) strains harbored the amino acid substitution R398M in the protein ERG11.

# Epidemiology – Mould fungaemia

**E1030**

## What is the epidemiology associated with mould-positive blood cultures? Ten-year data from 30 French centres

06. Fungal infection & disease
06a. Fungal disease epidemiology

T. Tala-Ighil [1], D. Garcia-Hermoso [2], S. Cassaing [3], A. Alanio [4], A. Xhaard [5], V. Bru [6], M.P. Ledoux [7], F. Dalle [8], M. Blot [9], T. Chouaki [10], A.P. Bellanger [11], L. Millon [11], C. Rouges [12], M.E. Bougnoux [13], M. Moniot [14], M. Pihet [15], V. Dubée [16], F. Gabriel [17], F. Morio [18], R. Le Floch [19], L. Hasseine [20], C. Bonnal [21], M. Gits-Muselli [22], E. Cateau [23], C. Mahinc [24], N. Desbois-Nogard [25], M. Nicolas [26], M. Demar [27], L. Epelboin [28], L. Kamus [29], E. Chachaty [30], C. Cordier [31], N. Bourgeois [32], L. Vincent [33], L. Courtemellont [34], B. Henry [35], F. Botterel [36], C. Angebault [37], L. Favennec [38], G. Gargala [39], G. Desoubeaux [40], M.L. Pacreau [41], J. Guitard [42], E. Dannaoui [13], F. Lanternier [1].

**RESSIF Network**
**France**
**2012-2022**

Table 1. Main epdemiological, microbiological and clinical characteristics of fungemia episodes

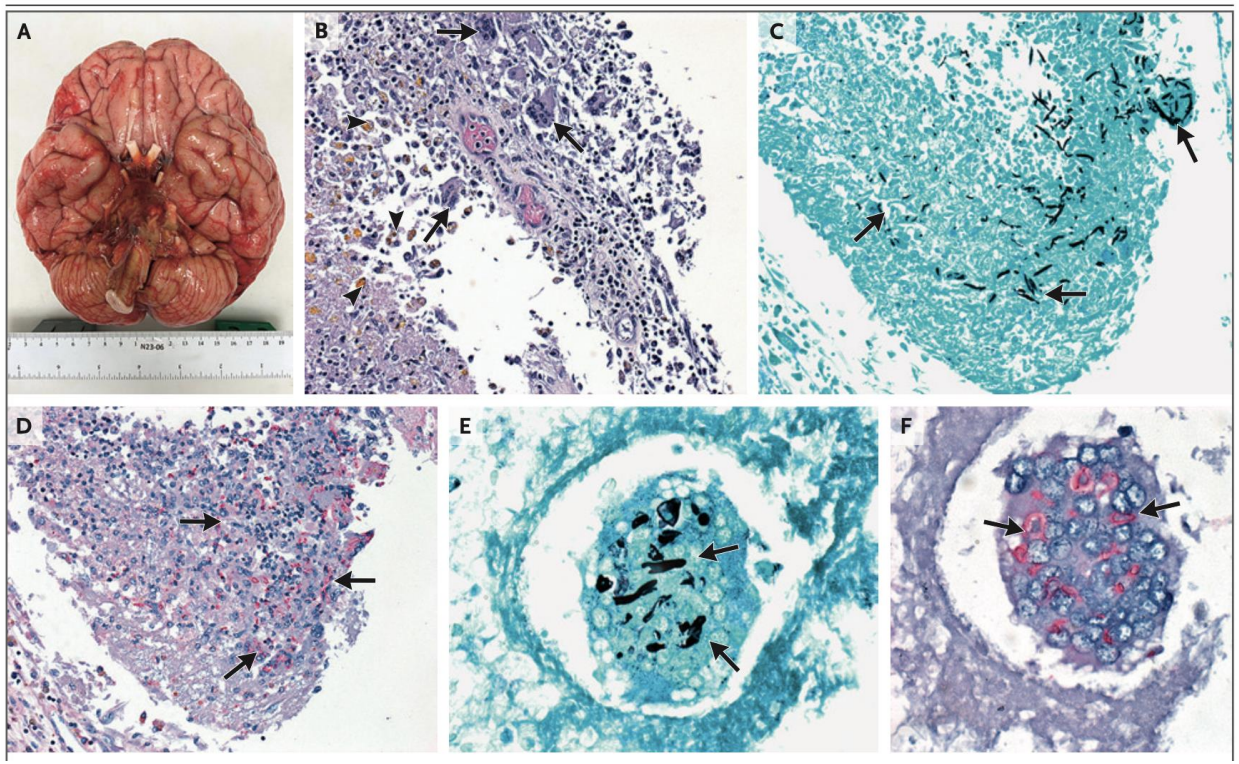
| | All (n=78) | *Fusarium* spp. (n=50) * | *Scedosporium/ Lomentospora* spp. (n=8)** | *Aspergillus* spp. (n=4) *** | *Mucor* spp. (n=5)[%] | *Trichoderma* spp. (n=5)[%%] | Other[%%%] (n=6) |
|---|---|---|---|---|---|---|---|
| **Sex (male) (n, %)** | 52 (66.7) | 32 (64.0) | 6 (75.0) | 3 (75.0) | 5 (100) | 2 (40.0) | 4 (66.7) |
| **Age (median, IQR°)** | 58.00 (26.25) | 57.50 (16.25) | 59.50 (15.5) | 57.50 (26.75) | 42.00 (63) | 38.00 (3) | 55.50 (5.5) |
| **Solid organ transplantation (SOT) [$] (n, %)** | 6 (7.7) | 1 (2.0) | 2 (25.0) | 1 (25.0) | 1 (20.0) | 0 (0) | 2 (33.3) |
| **Hematological malignancy (n, %)** | 51 (65.4) | 36 (72.0) | 6 (75.0) | 2 (50.0) | 2 (40.0) | 3 (60.0) | 2 (33.3) |
| HCST (n, %) | 20 (39.2) | 15 (41.7) | 3 (50.0) | 0 (0) | 0 (0) | 1 (33.3) | 1 (50.0) |
| Acute Lymphoblastic Leukeimia (n, %) | 7 (9.0) | 7 (19.4) | 1 (16.7) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| Acute Myeloblastic leukemia (n, %) | 14 (17.9) | 11 (30.6) | 2 (33.3) | 1 (50.0) | 1 (50.0) | 0 (0) | 0 (0) |
| Other [$$] (n,%) | 19 (24.4) | 10 (27.8) | 2 (33.3) | 1 (50.0) | 1 (50.0) | 3 (100) | 2(100) |
| **Neutropenia (> 10days < 500 G/l) (n, %)** | 37 (47.4) | 28 (56.0) | 4 (50.0) | 1 (25.0) | 0(0) | 2 (40.0) | 2 (33.3) |
| **Central veinous catheter (CVC) (n, %)** | 71 (91.0) | 44 (88.0) | 8 (100) | 4 (100) | 5 (100) | 5 (100) | 5 (83.3) |
| **Pulmonary involvement (n, %)** | 26 (33.3) | 16 (32.0) | 5 (83.3) | 1 (25.0) | 2 (40.0) | 1 (20.0) | 1 (16.7) |
| **Cutaneous involvement (n, %)** | 26 (33.3) | 20 (40.0) | 3 (50.0) | 1 (25.0) | 1 (20.0) | 0 (0) | 1 (16.7) |
| **Fungemia duration (mean +/- sd°°) (days)** | 2.4 (1.8) | 2.0 (1.8) | 4.1 (4.5) | 1.0 (0) | 2.0 (1.0) | 1.0 (1.8) | 5.5 (1.8) |
| **Positive central blood culture (n, %)** | 54 (69.2) | 35 (70.0) | 5 (71.4) | 3 (75.0) | 3 (60.0) | 3 (60.0) | 5 (83.3) |
| **Central blood culture growth time (hours) (mean +/- sd°°)** | 67.2 (39.4) | 78.9 (31.32) | 66.0 (5.4) | 54.7 (19.4) | 35.9 (2.6) | 69.7 (4.0) | 107.9 (69.2) |
| **Positive peripheral blood culture (n, %)** | 33 (42.3) | 23 (46.0) | 4 (57.1) | 1 (25.0) | 1 (20.0) | 2 (40.0) | 2 (33.3) |
| **Peripheral blood culture growth time (hours) (mean +/- sd°°)** | 82.1 (42.1) | 85.6 (42.50) | 78.6 (11.7) | 172.0 (NA) | 49.3 (NA) | 55.7 (0.1) | 109.7 (NA) |
| **CVC ablation (n, %)** | 63 (80.8) | 41 (82.0) | 6 (85.7) | 3 (75.0) | 3 (60.0) | 5 (100) | 5 (83.3) |
| **Positive CVC culture (n, %)** | 17 (27.0) | 13 (31.7) | 2 (33.3) | 0 (0) | 1 (33.3) | 0 (0) | 1 (20.0) |
| **Pre-exposition to antifungal therapy in the last 30 days (n, %)** | 29 (37.2) | 21 (42.0) | 5 (62.5) | 1 (25.0) | 0 (0) | 1 (20.0) | 1 (16.7) |
| Lamb (n, %) | 7 (24.1) | 5 (23.8) | 2 (40.0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| Voriconazole (n, %) | 6 (20.7) | 5 (23.8) | 0 (0) | 0 (0) | 0 (0) | 1 (100) | 0 (0) |
| Posaconazole (n, %) | 12 (41.4) | 9 (42.9) | 2 (40.0) | 0 (0) | 0 (0) | 0 (0) | 1 (100) |
| Fluconazole (n, %) | 2 (6.9) | 1 (4.8) | 1 (20.0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| Other azole[µ] (n, %) | 2 (6.9) | 1 (4.8) | 0 (0) | 1 (100) | 0 (0) | 0 (0) | 0 (0) |
| Other [µµ] (n, %) | 9 (31.0) | 6 (28.6) | 2 (40.0) | 0 (0) | 0 (0) | 0 (0) | 1 (100) |
| **Survival day 14 (n, %)** | 47 (60.3) | 34 (68.0) | 1 (12.5) | 2 (50.0) | 1 (20.0) | 3 (60.0) | 6 (100) |
| **Survival day 90 (n, %)** | 36 (46.2) | 28 (56.0) | 0 (0) | 0 (0) | 1 (20.0) | 2 (40.0) | 5 (83.3) |

# Investigation of fungal outbreaks – *F. solani*

ID, neutropenia

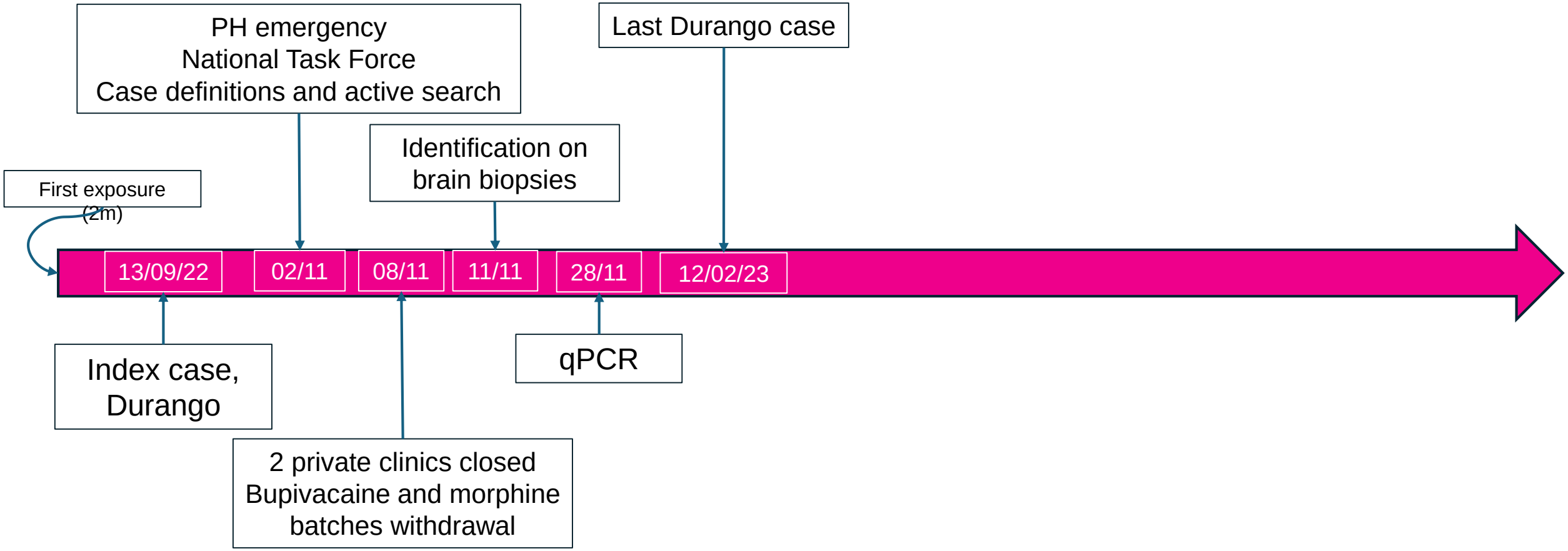
Environmental contamination

1-3% IFD in HSCT




Strong N, et al. NEJM 2024.

# Investigation of fungal outbreaks – *F. solani*




M. Fernandez Gonzalez Laura, ECCMID 2024. Garcia Rodriguez G, et al. OFID 2023.

# Investigati

PH emergency
National Task Force
Case definitions and active search

Identification on brain biopsies

First exposure (2m)

13/09/22 | 02/11 | 08/11 | 11/11 | 28

Index case, Durango

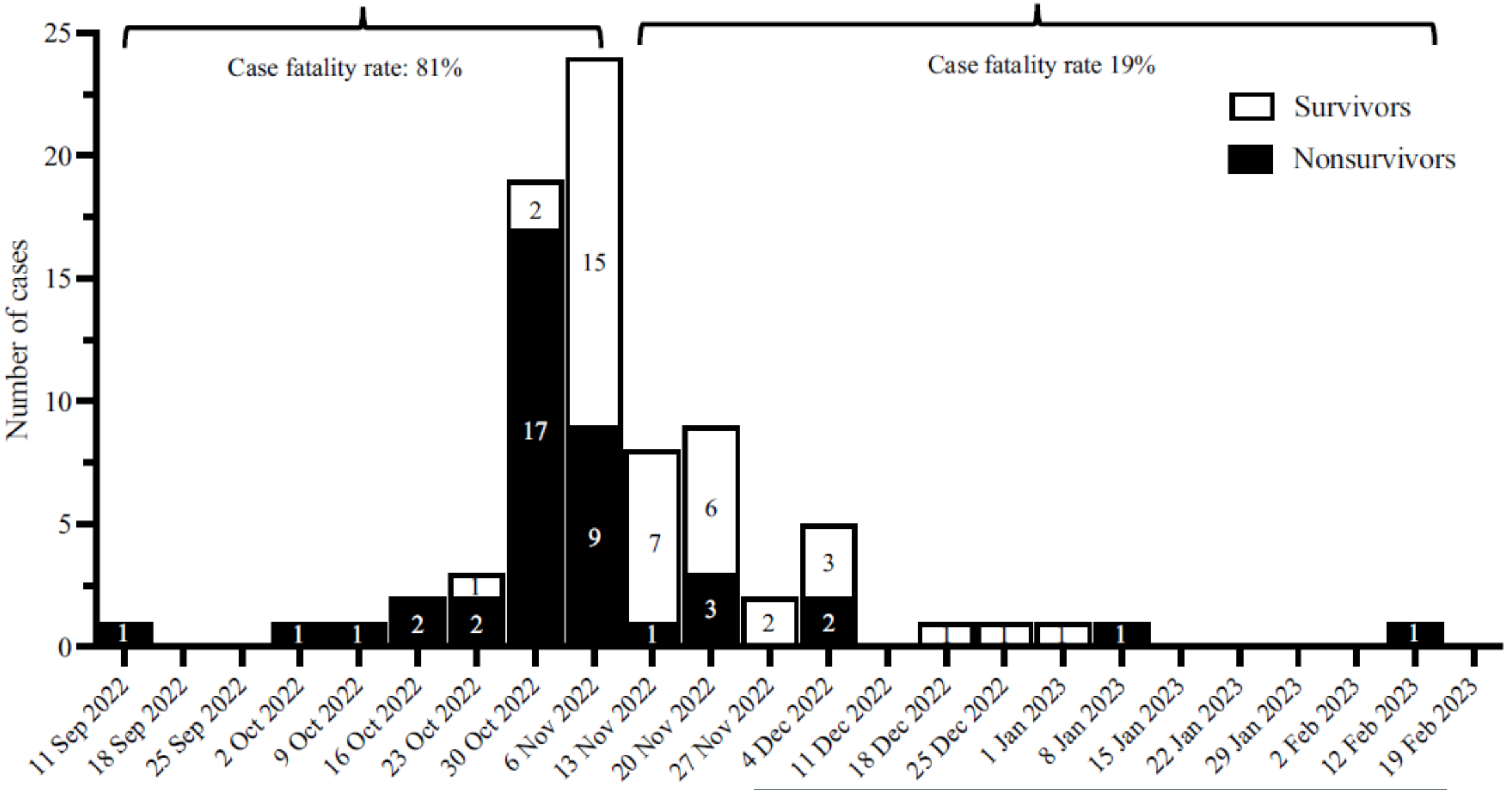
2 private clinics closed
Bupivacaine and morphine batches withdrawal

qP

**Table 2. Demographic and Clinical Data From Patients With Meningitis Associated With *Fusarium solani* Infection (N = 80)**

| Characteristic | Total | Nonsurvivors | Survivors | *P* Value |
|---|---|---|---|---|
| Meningitis cases, No. (%) | 80 (100) | 41 (51.3) | 39 (48.7) | |
| Age, y, median (IQR) | 30 (24.7–36.2) | 30 (22.5–35) | 30 (25–37.2) | .942[a] |
| Female, No. (%) | 76 (95) | 40 (97.6) | 36 (92.3) | .353[b] |
| Surgical procedures, No. (%) | | | | |
| Cesarean section | 61 (76.3) | 33 (80.5) | 28 (71.8) | .258[b] |
| Cholecystectomy | 3 (5.1) | 2 (4.9) | 1 (2.6) | |
| Knee arthroplasty | 3 (3.8) | 2 (4.9) | 1 (2.6) | |
| Hysterectomy | 2 (2.5) | 0 (0) | 2 (5.1) | |
| Ovarian cystectomy | 2 (2.5) | 2 (4.9) | 0 (0) | |
| Natural childbirth | 2 (2.5) | 0 (0) | 2 (5.1) | |
| Orchiectomy | 2 (2.5) | 0 (0) | 2 (5.1) | |
| Bilateral tubal occlusion | 1 (1.3) | 0 (0) | 1 (2.6) | |
| Colpoperineoplasty | 1 (1.3) | 0 (0) | 1 (2.6) | |
| Hysteroscopy | 1 (1.3) | 0 (0) | 1 (2.6) | |
| Osteosynthesis removal | 1 (1.3) | 1 (2.4) | 0 (0) | |
| qPCR results, No. (%) | | | | |
| Positive | 31 (38.8) | 19 (46.3) | 12 (30.8) | **<.001**[b] |
| Negative | 26 (32.5) | 2 (4.9) | 24 (61.5) | |
| Without qPCR | 23 (28.7) | 20 (48.8) | 3 (7.7) | |
| Time periods, median (IQR) | | | | |
| Incubation days[c] | 7 (4–30) | 7 (4–30.5) | 7 (3.7–25.7) | .836[a] |
| Days of hospitalization[d] | 39.5 (18–86.5) | 50.5 (18.7–84.5) | 38 (18–93) | .338[a] |
| Days since surgery to hospitalization | 78 (52.5–99.7) | 76 (55.5–93.5) | 80 (38–126) | .149[a] |
| Antifungal onset[e], days | 4 (2–9) | 7 (3–11.7) | 3.5 (2–6.2) | **.018**[a] |
| Patient management, No. (%) | | | | |
| Admission to the ICU | 36 (45) | 34 (82.9) | 2 (5.1) | **<.001**[b] |
| Treatment with voriconazole and AmB | 71 (88.8) | 35 (85.4) | 36 (92.3) | .483[b] |
| Treatment with steroids | 64 (80) | 35 (85.4) | 29 (74.3) | .122[b] |

Attack rate 4.5%. Mortality 51.3%
Only 3 cases with positive CSF culture



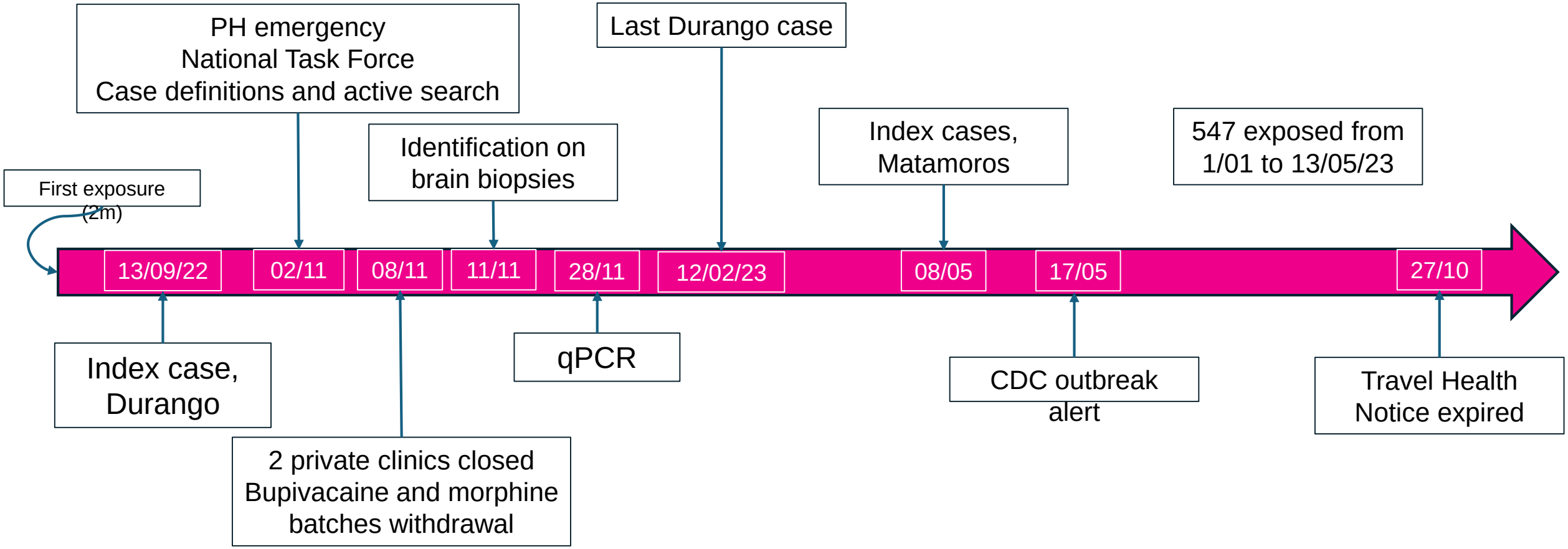

| *P* Value |
|---|
| |
| .942[a] |
| .353[b] |
| .258[b] |
| **<.001**[b] |
| .836[a] |
| .338[a] |
| .149[a] |
| **.018**[a] |
| **<.001**[b] |
| .483[b] |
| .122[b] |

# Outbreak investigation

- Private clinics from the same owner with an high frequency of Ab&Gyn procedures at accessible costs
- Breaches in IPC practices, possible drug contamination during preparation and storage (**no microbiological confirmation**)
- Environmental factors (dus and wind) may have increased fungal load in the air

El Siglo de Durango. May 19,2022

# Investigation of fungal outbreaks – *F. solani*




M. Fernandez Gonzalez Laura, ECCMID 2024. Garcia Rodriguez G, et al. OFID 2023.

# In
—

Na
Case defi

First exposure
(2m)

13/09/22

Index cas
Durango

27/10

vel Health
ce expired

U.S. Cases under Investigation, Case Counts, and Deaths as of 8/31/23

| Case Types | Case Counts |
|---|---|
| **Persons under investigation** (**People with no symptoms**[1] or symptoms are unknown, spinal tap results pending or unknown) | 151 |
| **Suspected cases** (Symptoms consistent with meningitis, spinal tap results pending or unknown) | 9 |
| **Probable cases** (**Spinal tap results suggest meningitis**;[2] fungus not isolated) | 14 |
| **Confirmed cases** (Fungus detected from samples[3]) | 10 |
| **Deaths**[4] | 12 |

[1] Meningitis symptoms include fever, headache, stiff neck, nausea, vomiting, photophobia, and altered mental status.

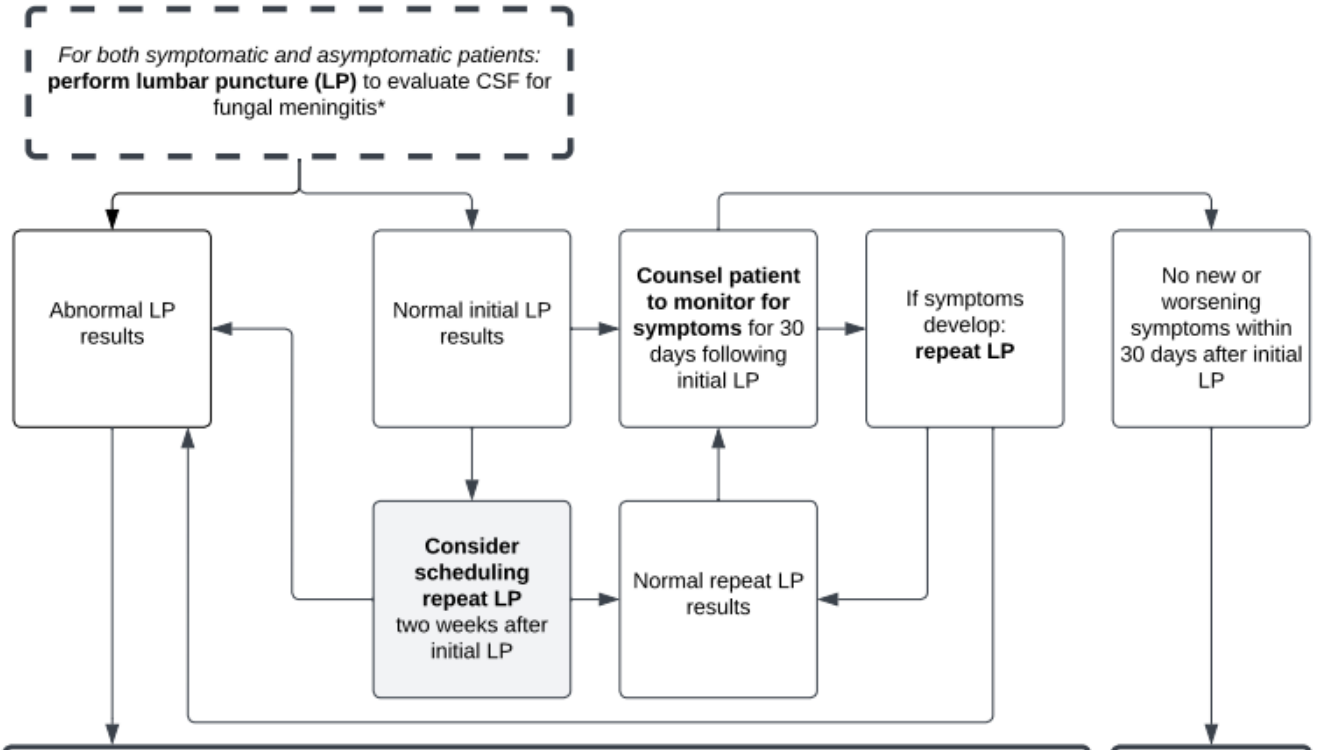
[2] Cerebrospinal fluid (CSF) profile with >5 WBCs/mm$^3$, accounting for the presence of red cells (i.e., subtracting 1 white cell for every 500 RBCs present).

[3] Fungus could be detected by culture, polymerase chain reaction (PCR) testing, or metagenomic next generation sequencing (mNGS) testing of CSF or tissue. Only select laboratories in the U.S. can test for the type of fungi involved in this outbreak creating a lag time between the spinal tap and receiving results.

[4] Three probable cases and nine confirmed cases.

# Evaluating and Treating Patients for Fungal Meningitis

Patients at risk for fungal meningitis include those who received epidural anesthesia from Jan. 1, 2023 to May 13, 2023 at Riverside Surgical Center or Clinica in K-3, in Matamoros, Mexico.




- **Begin antifungal therapy:** minimum of 2 weeks dual antifungal therapy with IV liposomal amphotericin B (AmBisome®) and voriconazole.
- A **minimum of 3 months antifungal therapy is recommended**, but therapy may be needed for >6 months in severe cases
- Check serum voriconazole trough level (target 4–5 mcg/ml) on the 5th day of voriconazole treatment (and at least weekly thereafter)
- Step-down to voriconazole monotherapy depends on clinical improvement and CSF profile improvement
- **MRI brain (w/wo contrast) is recommended** to assess for meningeal enhancement, vasculitis, stenosis, hemorrhage, or ischemia
- **Early and close consultation with an infectious diseases specialist** and **neurologist** is recommended
- Monitor for fungal meningitis complications (stroke, increased intracranial pressure, brain edema), which indicate a worse prognosis
- Hospital discharge depends multiple factors including: (1) clinical improvement; (2) CSF profile improvement; and (3) ability to ensure close clinical follow-up including serum voriconazole level monitoring and liver and kidney function

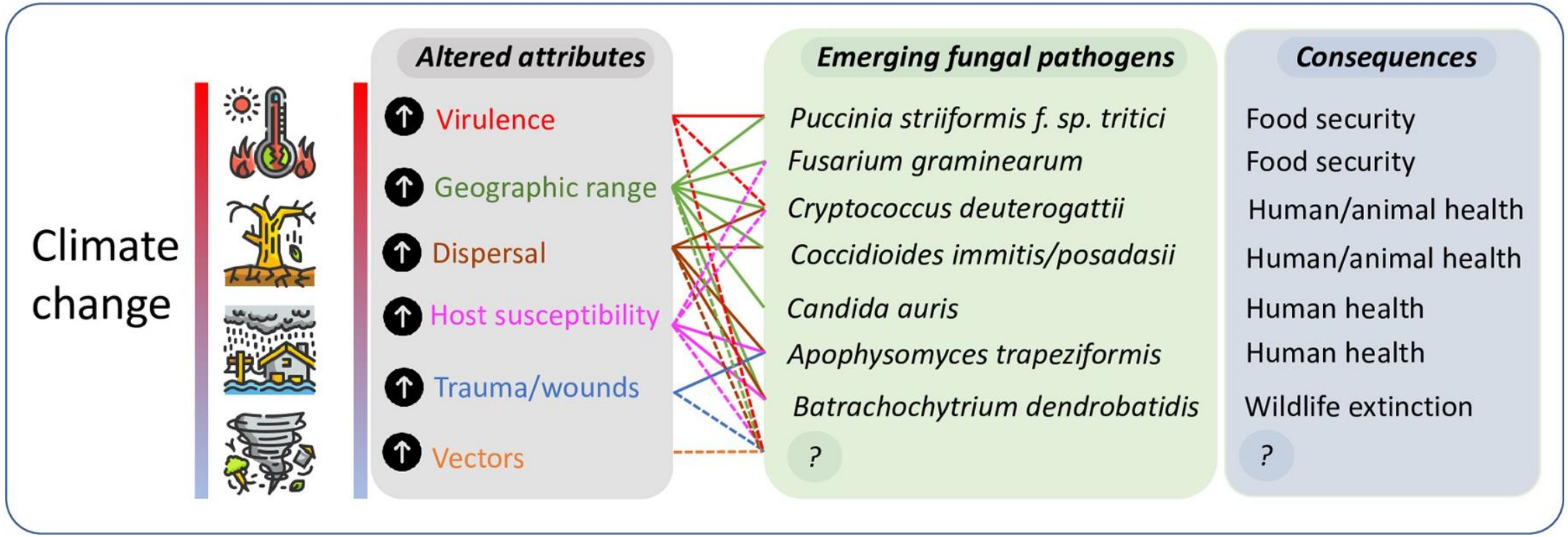
No fungal meningitis: **evaluation complete**

# Outbreak investigation phases

1. Establish the existence of an outbreak (definition)
2. Confirm the diagnosis
3. Establish case definition and find cases sistematically (passive/active surveillance)
4. Perform descriptive epidemiology (epi curve, maps)
5. Determine the population at risk (denominator)
6. Develop and test hypotheses
7. Environmental sampling, if necessary
8. Compare and reconcile with previous studies
9. Communicate findings, written report
10. Implement IPC measures

Gregg, Michael B. (Editor). Field Epidemiology.Oxford University Press, new York, 1996.

# Climate change

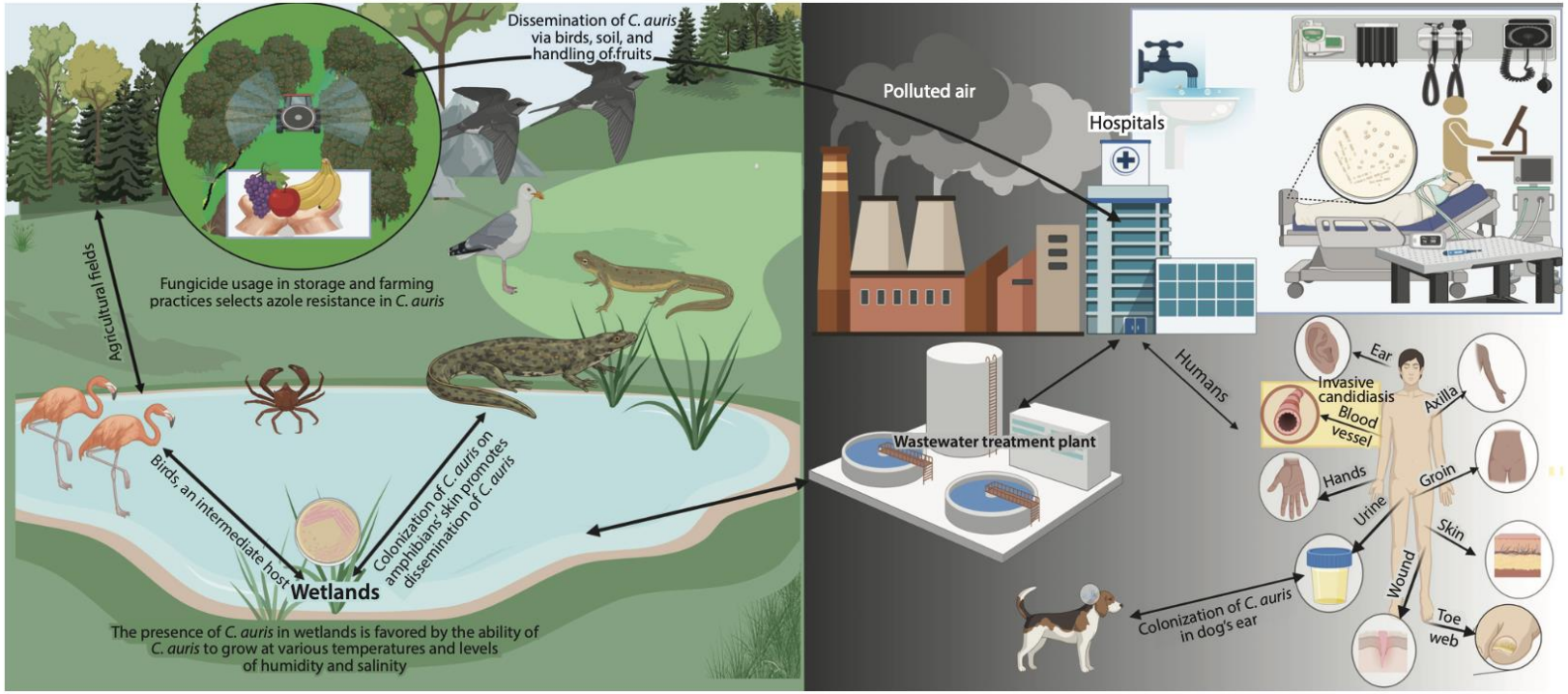



New habitats for fungi, dispersion/vector/vehicles, brach host physical barriers

# *Candida auris*

## A new species (the first?) emerged due to climate change

In 2021, the isolation of wild *C. auris* from a salt marsh and a sandy beach on the Andaman Islands in the Indian Ocean provided the first confirmation of the environmental niche of *C. auris* and its association with a marine ecosystem.



# Diagnosis – PCP

Detection of *P. jirovecii* from respiratory samples (BAL, induced sputum, sputum, tracheal aspirate…)

- Microscopy with silver staining or fluorescent brightners (no culture) (HIV)
- Conventional or real-time PCR (cPCR or qPCR)

Detection of *P. jirovecii* in blood: PCR

Detection of fungal glucan in blood: BDG (high NPV)

Clinical Infectious Diseases

MAJOR ARTICLE

# Polymerase Chain Reaction on Respiratory Tract Specimens of Immunocompromised Patients to Diagnose *Pneumocystis* Pneumonia: A Systematic Review and Meta-analysis

Lottie Brown,[1] Riina Rautemaa-Richardson,[2] Carlo Mengoli,[3] Alexandre Alanio,[4] Rosemary A. Barnes,[5] Stéphane Bretagne,[6] Sharon C.-A. Chen,[7] Catherine Cordonnier,[8] J. Peter Donnelly,[9] Werner J. Heinz,[10] Brian Jones,[11] Lena Klingspor,[12] Juergen Loeffler,[13] Thomas R. Rogers,[14] Eleanor Rowbotham,[15] P. Lewis White,[16] and Mario Cruciani[9]

To examine the comparative diagnostic performance of PCR and sampling approaches, in both HIV and non-HIV populations with **proven** PCP.

Eligible studies:

- PCR compared with microscopy (**proven**, EORCT)
- Results reported as TP, FP, FN. TN
- Population of patients at risk for PCP with clinical suspicion

55 studies, 7835 patients, 11434 PCR assays
34.8 % PLWH, 12.8% HM, 5.9% SOT
PCP mean prevalence 20.7%

**Table 1. Sensitivity, Specificity, and Diagnostic Odds Ratio of Polymerase Chain Reaction (PCR) Test According to PCR Technique**

| Sample | Sensitivity (95% CI) | Specificity (95% CI) | DOR (95% CI) | $LR^+$ (95% CI) | $LR^-$ (95% CI) |
|---|---|---|---|---|---|
| BALF samples | | | | | |
| qPCR (n = 2673) | 0.987 (.968–.995) | 0.893 (.844–.927) | 635 (269–1498) | 9.194 (5.727–12.661) | 0.014 (.001–.027) |
| cPCR (n = 2254) | 0.972 (.932–.988) | 0.954 (.930–.970) | 710 (305–1652) | 21.178 (12.438–29.918) | 0.30 (.004–.056) |
| IS samples | | | | | |
| qPCR (n = 491) | 0.980 (.944–.993) | 0.815 (.721–.883) | 217 (78–601) | 5.303 (3.024–7.583) | 0.024 (.000–.049) |
| cPCR (n = 590) | 0.956 (.887–.984) | 0.917 (.866–.950) | 243 (90–656) | 11.511 (5.985–17.036) | 0.047 (.001–.094) |
| URT samples | | | | | |
| qPCR (n = 352) | 0.892 (.710–.965) | 0.905 (.809–.955) | 78 (26–238) | 9.340 (2.997–15.682) | 0.120 (NE–.245) |
| cPCR (n = 512) | 0.787 (.502–.931) | 0.960 (.911–.982) | 87 (27–284) | 19.424 (5.358–33.490) | 0.222 (NE–.446) |

# Diagnosis - PCP

| |
|---|
| qPCR has optimal Sn and good Sp both in BAL and IS |
| No difference according to HIV status |
| qPCR should be preferred over cPCR if available |
| qPCR can detect lower fungal (colonization? lower Sp than cPCR) |
| Sp is more variable than Sn in studies, prefer »targeted» samples (BAL) |




*Clinical Infectious Diseases*

MAJOR ARTICLE

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

Sejal Morjaria,[1,2] John Frame,[3] Alexandra Franco-Garcia,[1] Alexander Geyer,[2,4] Mini Kamboj,[1,2] and N. Esther Babady[1,5]

Modified from Alanio A, *et al. J Antimicrob Chemother* 2016;71:2386–2396.

Clinical findings + PCR pos + BDG >200 pg/mL → Sp 100% for PCP in ID

# Diagnosis – New GM Kit

The VirCLIA® GM assay (Vircell) is an automated chemiluminescence immunoassay (CLIA) for individual samples (serum or BAL) and provides quantitative results in 1.5 h.

Predefined manufacturer's cut-off values are > 0.200 for positive, < 0.160 for negative and 0.160 - 0.200 for undetermined values.

In BAL: Sn 61%, Sp 100%; strong correlation, qualitative agreement *

*Buil JB, et al. JCM 2023.

O1195

# Multi-centre evaluation of a commercial galactomannan assay on serum in two cohorts of haematology patients with suspected invasive fungal disease

06. Fungal infection & disease
06b. Diagnostic mycology (incl traditional, molecular and other methods)

H. Lamberink [1], S. Huygens [1], R. Aerts [2], K. Van Dijk [3], D. Langerak [1], I. Moors [4], J. Boelens [4], M. Reynders [5], K. Lagrou [2], A. Schauwvlieghe [5], M. Van Westreenen [1], G.L. Chong [1], P. Verweij [6], J. Buil [6], B. Rijnders [1].

*[1]Erasmus MC - Rotterdam (Netherlands), [2]UZ Leuven - Leuven (Belgium), [3]Amsterdam UMC - Amsterdam (Netherlands), [4]UZ Gent - Ghent (Belgium), [5]AZ St-Jan - Bruges (Belgium), [6]Radboud UMC - Nijmegen (Netherlands)*

- Validation study of VirCLIA on serum in two independent cohorts
- Study population: HM, lesion on HRCT, BAL
- CLIA (VirCLIA) vs. EIA (PlateliaTM)
- Cases (proven/probable IA) vs. controls (possible/no IA); EORTC 2020

O1195

# Multi-centre evalua … cohorts of haematology patien…

06. Fungal infection & dis…
06b. Diagnostic mycolog…

H. Lamberink [1], S. Huygens [1], R. … lieghe [5], M. Van Westreenen [1], G.L. Chong [1], P. V…
[1]Erasmus MC - Rotterdam (Neth… - Ghent (Belgium),
[5]AZ St-Jan - Bruges (Belgium),

Table 1. Baseline characteristics

| | All patients (n=353) Median (IQR) and/or *n* (%) | Cohort 1 (n=163) Median (IQR) and/or *n* (%) | Cohort 2 (n=190) Median (IQR) and/or *n* (%) |
|---|---|---|---|
| **Age, y** | 61 (52.5-68.0) | 63 (54.0-70.0) | **60 (50.0-68.0)** |
| **Sex, male** | 222/353 (62.9) | 109/163 (66.9) | **113/190 (59.5)** |
| **Underlying hematological malignancy** | 353/353 (100) | 163/163 (100) | **190/190 (100)** |
| AML | 175 (49.6) | 77 (47.2) | **98 (51.6)** |
| MDS | 38 (10.8) | 15 (9.2) | **23 (12.1)** |
| ALL | 28 (7.9) | 13 (8.0) | **15 (7.9)** |
| Other | 112 (31.7) | 58 (35.6) | **54 (28.4)** |
| **SCT** | 123/348 (35.3) | 50/158 (31.6) | **73/190 (38.4)** |
| Allogeneic | 110 (31.6) | 43 (27.2) | **67 (35.3)** |
| Autologous | 13 (3.7) | 7 (4.4) | **6 (3.2)** |
| None | 225 (63.7) | 108 (68.4) | **117 (61.6)** |
| **Neutropenia[1]** | 159/295 (53.9) | 51/105 (48.6) | **108/190 (56.8)** |
| **No AFT[2]** | 123/287 (42.9%) | 34/97 (35.1) | **89/190 (46.8)** |
| Fluconazole | 70 (24.4) | 37 (38.1) | **33 (17.4)** |
| Anti-mould AFT | 94 (32.6) | 26 (26.8) | **68 (35.8)** |
| Voriconazole | 33 (11.5) | 13 (13.4) | **20 (10.5)** |
| Posaconazole | 11 (3.8) | 3 (3.1) | **8 (4.2)** |
| Isavuconazole | 12 (4.2) | 0 (0) | **12 (6.3)** |
| Echinocandins | 5 (1.7) | 2 (2.1) | **3 (1.6)** |
| L-AmB | 15 (5.2) | 2 (2.1) | **13 (6.8)** |
| Combination therapy | 15 (5.2) | 6 (6.2) | **9 (4.7)** |
| Other | 3 (1.0) | 0 (0) | **3 (1.6)** |
| **Fungal diagnostics (positive findings)** | | | |
| BAL microscopy[3] | 20/222 (9.0) | 10/131 (7.6) | **10/91 (11.0)** |
| BAL fungal culture | 31/244 (12.7) | 19/152 (12.5) | **12/92 (13.0)** |
| BAL GM (EIA, =1.00), frequency | 79/218 (36.2) | 46/148 (31.1) | **33/70 (47.1)** |
| BAL GM (EIA), ODI | 0.43 (0.10-2.63) | 0.30 (0.10-2.17) | **0.64 (0.10-3.50)** |
| BAL PCR (duplicate) | 98/212 (46.2) | 62/133 (46.6) | **36/79 (45.6)** |
| **EORTC/MSGERC criteria[4]** | 353 | 163 | **190** |
| Proven IA | 11 (3.1) | 6 (3.7) | **5 (2.6)** |
| Probable IA | 123 (34.8) | 67 (41.1) | **56 (29.5)** |
| Possible IA | 98 (27.8) | 68 (41.7) | **30 (15.8)** |
| No IA/unclassifiable | 117 (33.1) | 22 (13.5) | **95 (50.0)** |

Validation study c…

Study popu…

CLI…

…); EORTC

Positive/negative agreement: 65.8/96.2%, overall > 93%.

| | Sensitivity cohort 1 (%) | Sensitivity cohort 2 (%) | Specificity cohort 1 (%) | Specificity cohort 2 (%) | PPV cohort 1 (%) | PPV cohort 2 (%) | NPV cohort 1 (%) | NPV cohort 2 (%) |
|---|---|---|---|---|---|---|---|---|
| GM ELISA ≥1.0 | 21.1 | 33.3 | 100.0 | 99.2 | 100.0 | 95.5 | 61.6 | 74.9 |
| GM ELISA ≥0.5 | 36.6 | 49.2[1] | 95.6 | 96.8[2] | 86.7 | 88.6 | 65.7 | 79.2 |
| GM CLIA ≥0.2 | 11.3 | 38.1 | 97.8 | 99.2 | 80.0 | 96.0 | 58.3 | 76.2 |
| GM CLIA ≥0.16 | 16.9 | 47.6 | 97.8 | 96.8 | 85.7 | 88.2 | 59.9 | 78.7 |
| GM CLIA ≥0.10 | 35.2 | 61.9[1] | 85.6 | 90.5[2] | 65.8 | 76.5 | 62.6 | 82.6 |

CLIA and EIA showed qualitative and quantitative agreement

Excellent discrimination power with regard to EORTC 2020 criteria

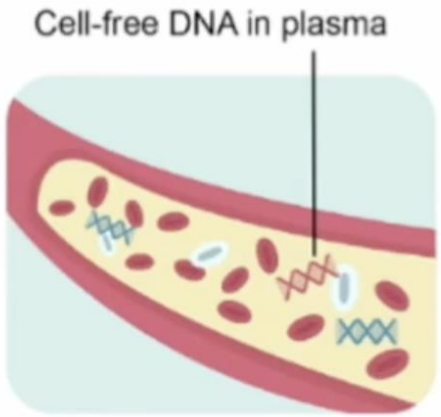
Lowering CLIA cut-off to 0.100 improves Sn without compromising Sp

Low reproducibility results of results between 0.100 and 0.200

To be used in population with high pre-test probability

# Diagnosis – Mould cfDNA PCR

- Targeted PCR (Multiplex)
  - *Aspergillus* spp. (*fumigatus/niger/flavus*)
  - *Aspergillus terreus/ustus*
  - Mucorales agents (*Rhizopus* spp., *Rhizomucor* spp., *Mucor* spp.)
  - *Scedosporium* spp./*Lomentospora prolificans*
  - *Fusarium* spp.

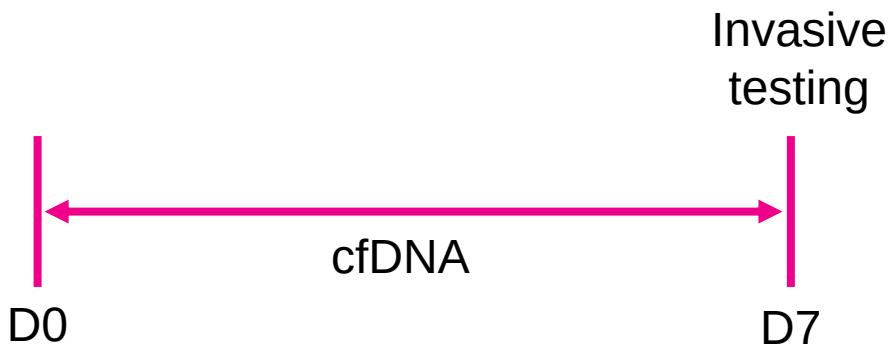



**Sn 86%, Sp 83% vs. GM ELISA**

Liu A, ECCMID 2024.

# Diagnosis – Mould cfDNA PCR

**It is still necessary to perform invasive testing for IFD?**




Cohort characteristics

Median age 55.0, (IQR 30.0-67.0)

61% male

87% immunocompromised

- 23% HSCT
- 30% SOT
- 44% HM
- 25% neutropenia

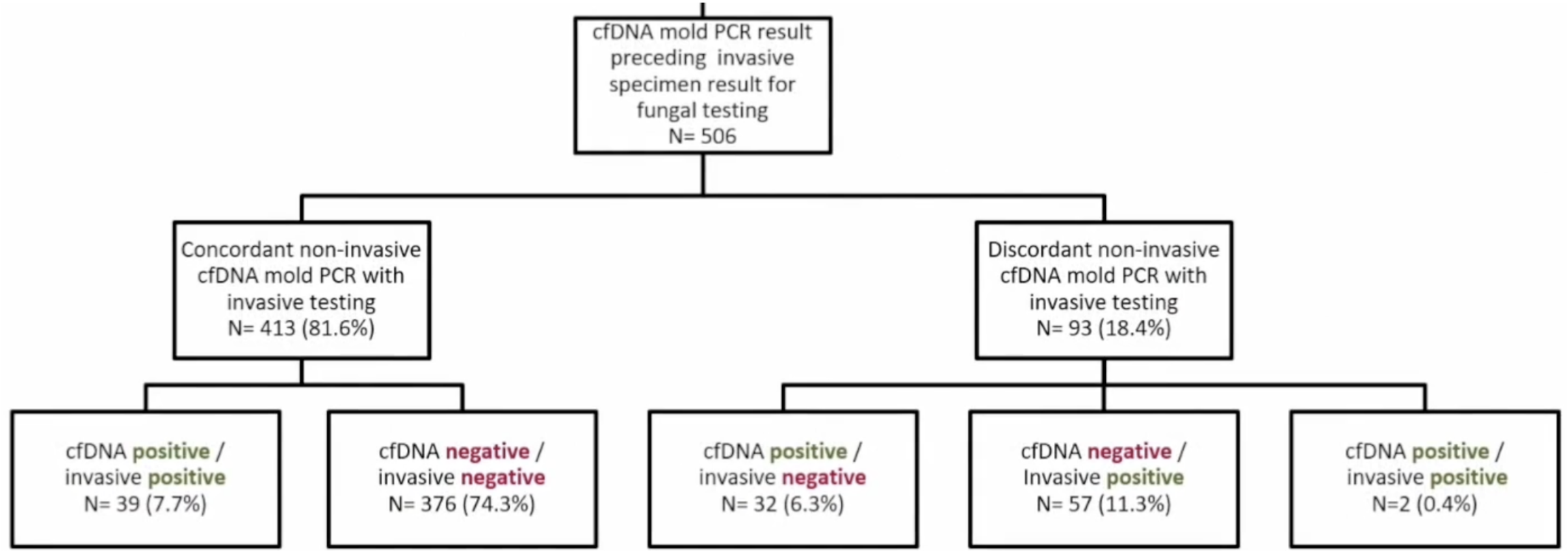
48% on prophylaxis

87% pulmonary infection

17% all cause-mortality at 30 days

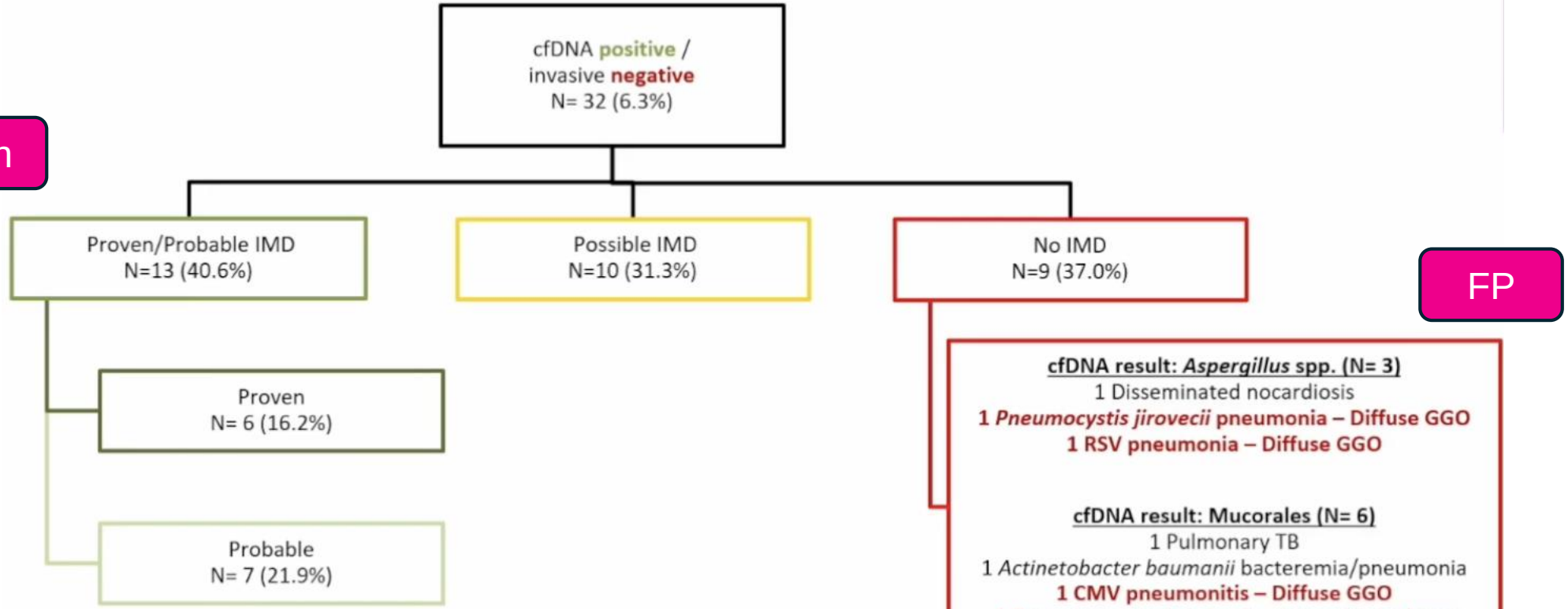
Liu A, ECCMID 2024.

# Diagnosis – Mould cfDNA PCR



# Diagnosis – Mould cfDNA PCR

Early detection

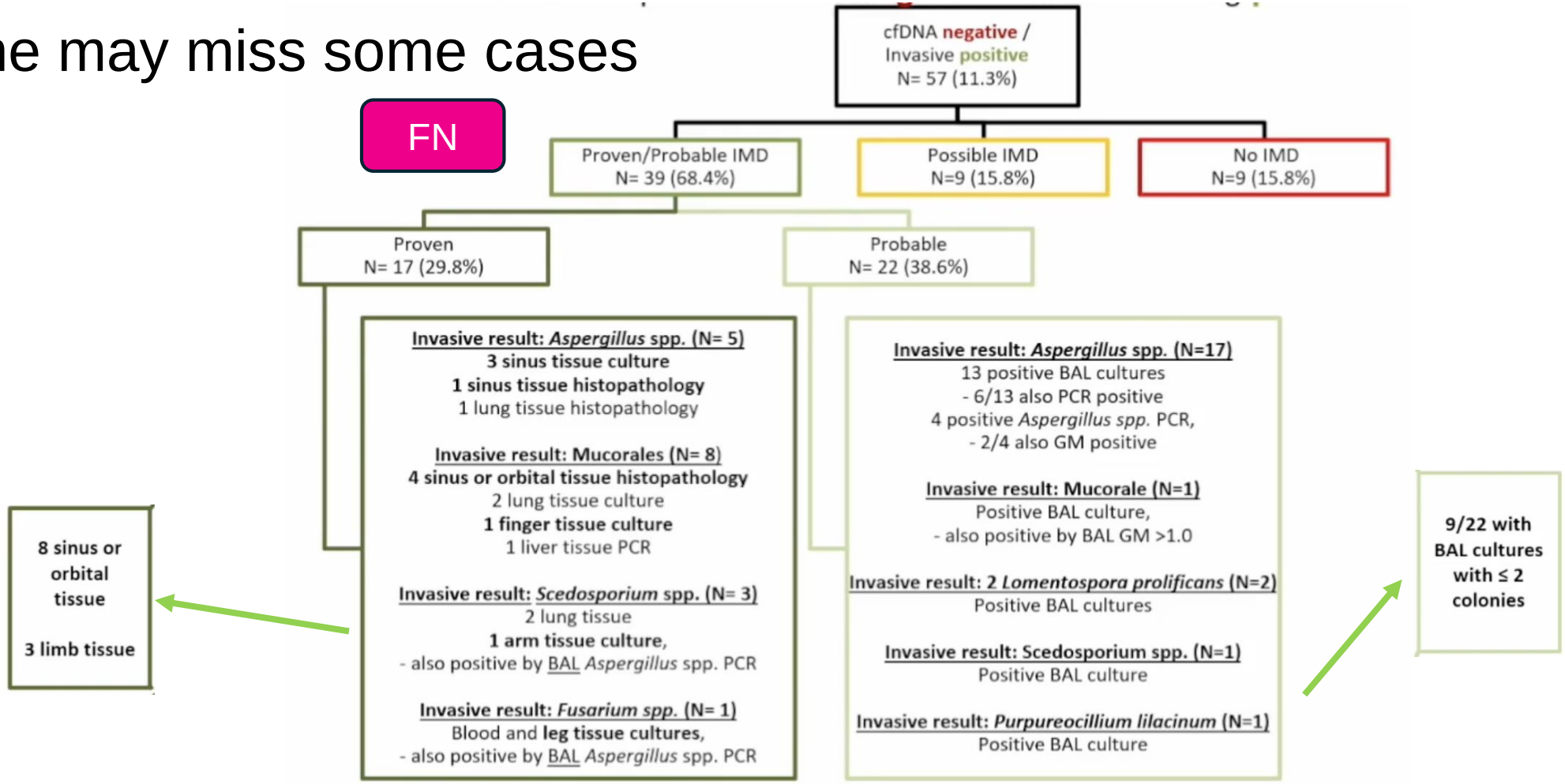



Liu A, ECCMID 2024.

# Diagnosis – Mould cfDNA PCR

cfDNA alone may miss some cases

FN

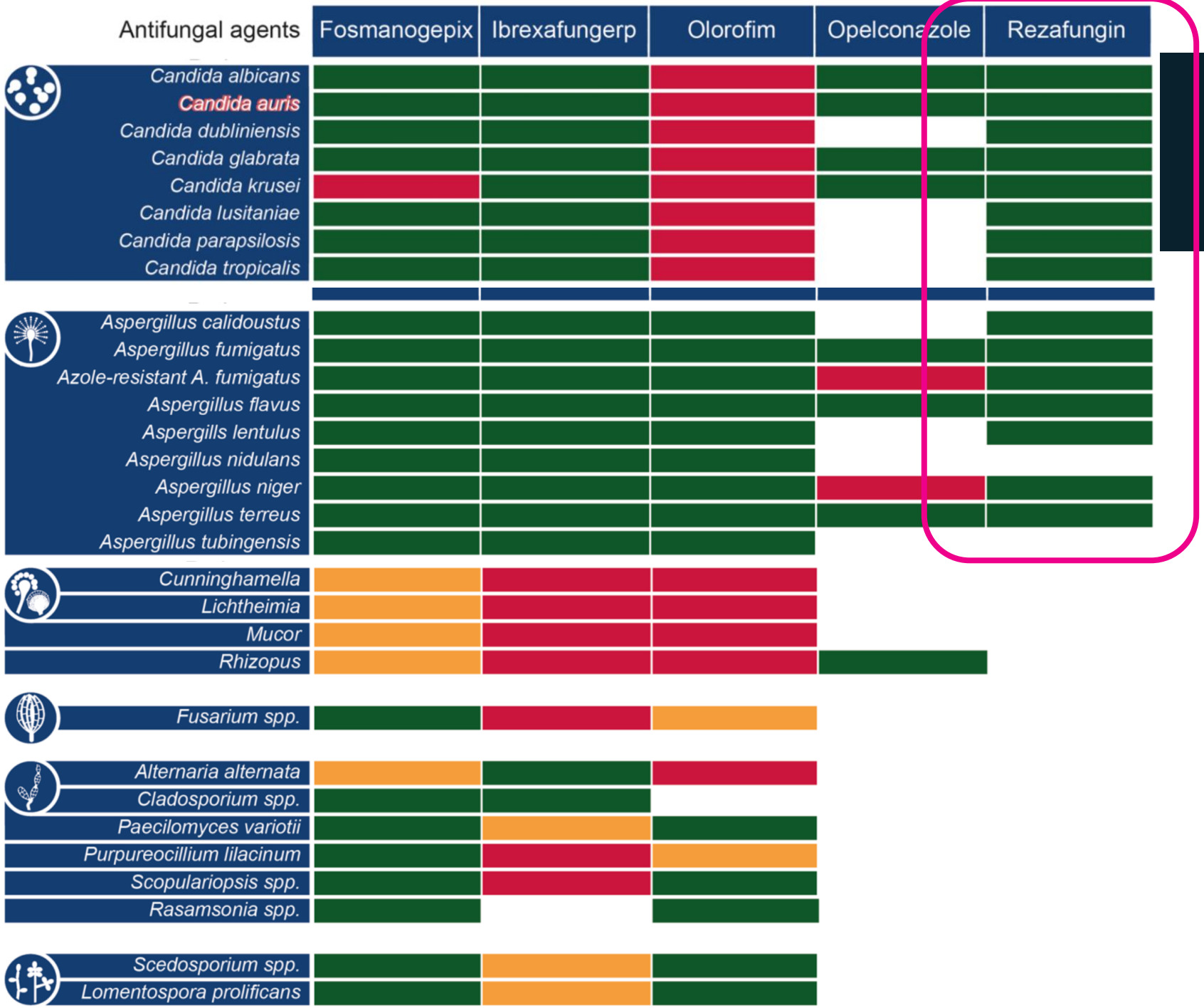



Liu A, ECCMID 2024.

# Diagnosis – Mould cfDNA PCR

- Excellent agreement (87.9%) with invasive testing for fungal testing. Potentially avoiding invasive procedures in many cases
- In high suspicion for IMD, particularly localized diseases (i.e. invasive fungal sinusitis) in non-neutropenic patient, invasive testing remains necessary.
- False positive, lack of clinical criteria (Laboratory stewardship)
- Higher diagnostic yield than serum GM

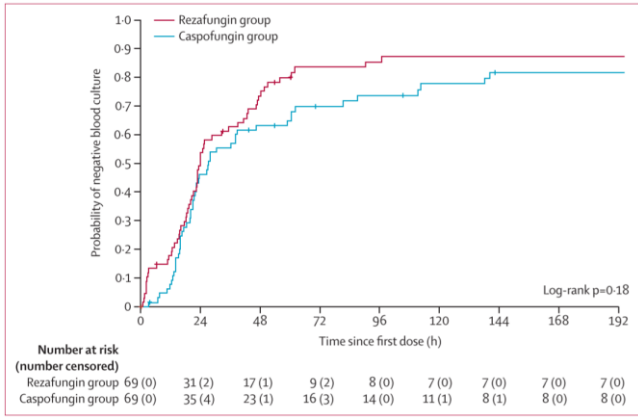
Liu A, ECCMID 2024.


Antifungal agents
Fosmanogepix
Ibrexafungerp
Olorofim
Opelconazole
Rezafungin
Candida albicans
Candida auris
Candida dubliniensis
Candida glabrata
Candida krusei
Candida lusitaniae
Candida parapsilosis
Candida tropicalis
Aspergillus calidoustus
Aspergillus fumigatus
Azole-resistant A. fumigatus
Aspergillus flavus
Aspergills lentulus
Aspergillus nidulans
Aspergillus niger
Aspergillus terreus
Aspergillus tubingensis
Cunninghamella
Lichtheimia
Mucor
Rhizopus
Fusarium spp.
Alternaria alternata
Cladosporium spp.
Paecilomyces variotii
Purpureocillium lilacinum
Scopulariopsis spp.
Rasamsonia spp.
Scedosporium spp.
Lomentospora prolificans

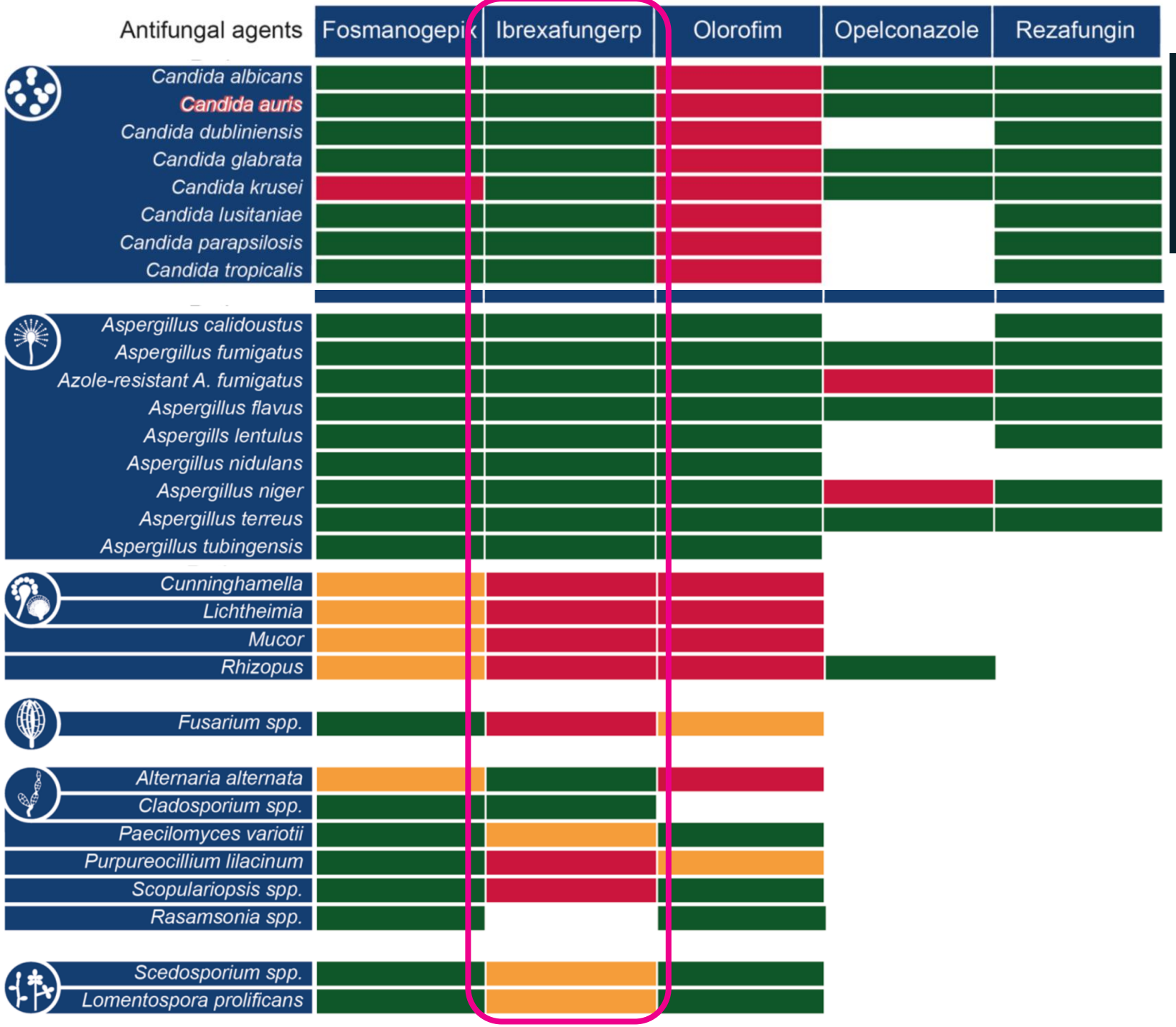
# Future treatment options - Rezafungin

| Future use | Advantages |
|---|---|
| Invasive *Candida* infections, deep-seated PCP? | Safe<br>Few DDI<br>q1w |

ReSPECT trial ongoing
NCT04368559: prevention of IFD in HSCT, vs. POS/FLU




| Substance | Latest study phase | FDA approval | EMA approval |
|---|---|---|---|
| Rezafungin | III Primary Tx for IC | ✓ For Invasive Candidiasis | ✓ For Invasive Candidiasis |
| Ibrexafungerp | III Stepdown Tx Candidemia | ✓ For VVC | ✗ Pending |
| CAmB | II | ✗ Pending | ✗ Pending |
| Oteseconazole | III Refractory VVC | ✓ For VVC | ✗ Pending |
| Olorofim | III (Salvage) Tx IA (OASIS) | ✗ Pending | ✗ Pending |
| Fosmanogepix | II | ✗ Pending | ✗ Pending |
| **Inhaled formulations** | | | |
| Opelconazole | III Refractory IPA | ✗ Pending | ✗ Pending |
| TFF Voriconazole | II | ✗ Pending | ✗ Pending |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Rezafungin
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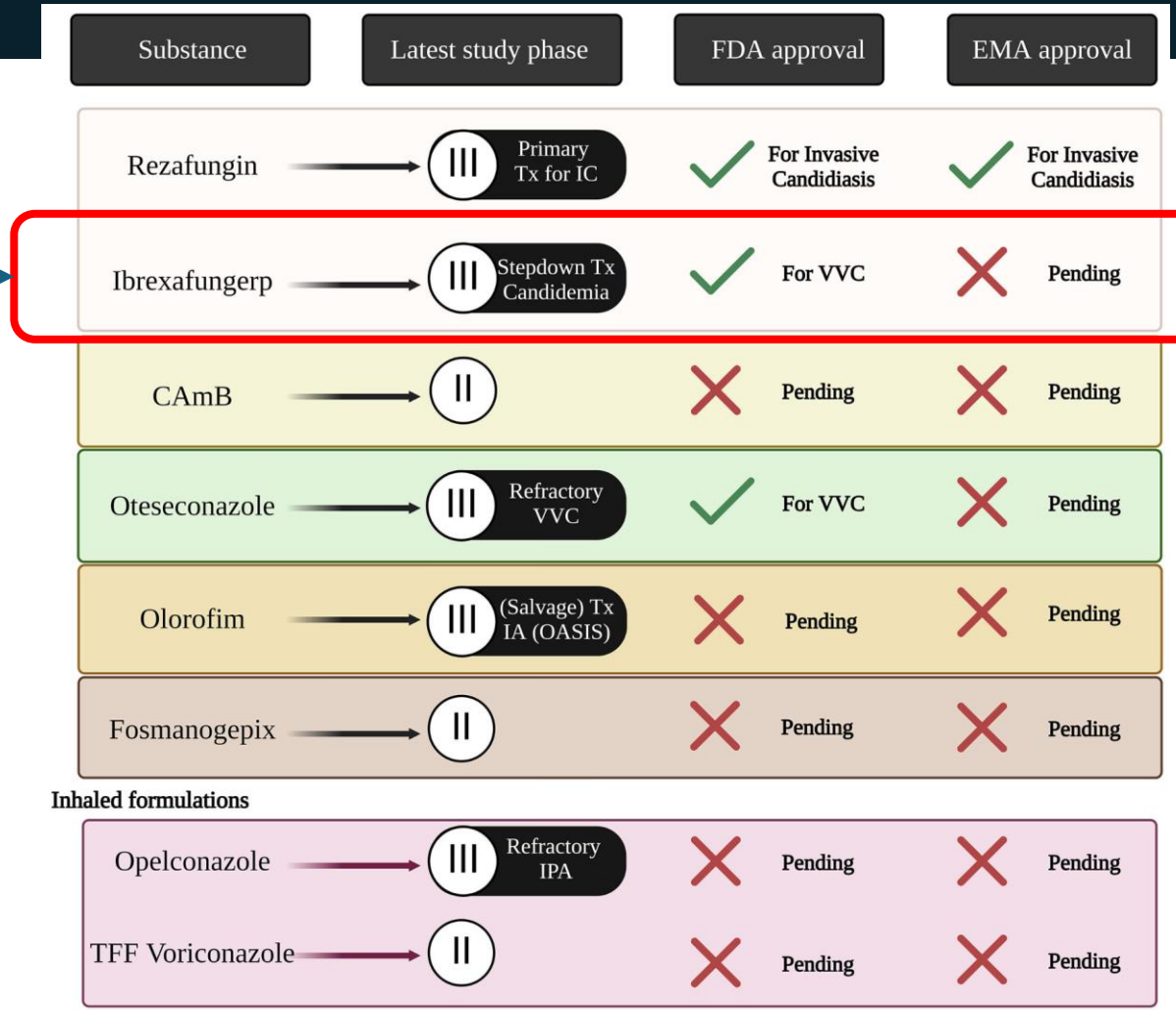
Candida dubliniensis
Candida glabrata
Candida krusei
Candida lusitaniae
Candida parapsilosis
Candida tropicalis
Aspergillus calidoustus
Aspergillus fumigatus
Azole-resistant A. fumigatus
Aspergillus flavus
Aspergills lentulus
Aspergillus nidulans
Aspergillus niger
Aspergillus terreus
Aspergillus tubingensis
Cunninghamella
Lichtheimia
Mucor
Rhizopus
Fusarium spp.
Alternaria alternata
Cladosporium spp.
Paecilomyces variotii
Purpureocillium lilacinum
Scopulariopsis spp.
Rasamsonia spp.
Scedosporium spp.
Lomentospora prolificans

# Future treatment options – Ibrexafungerp

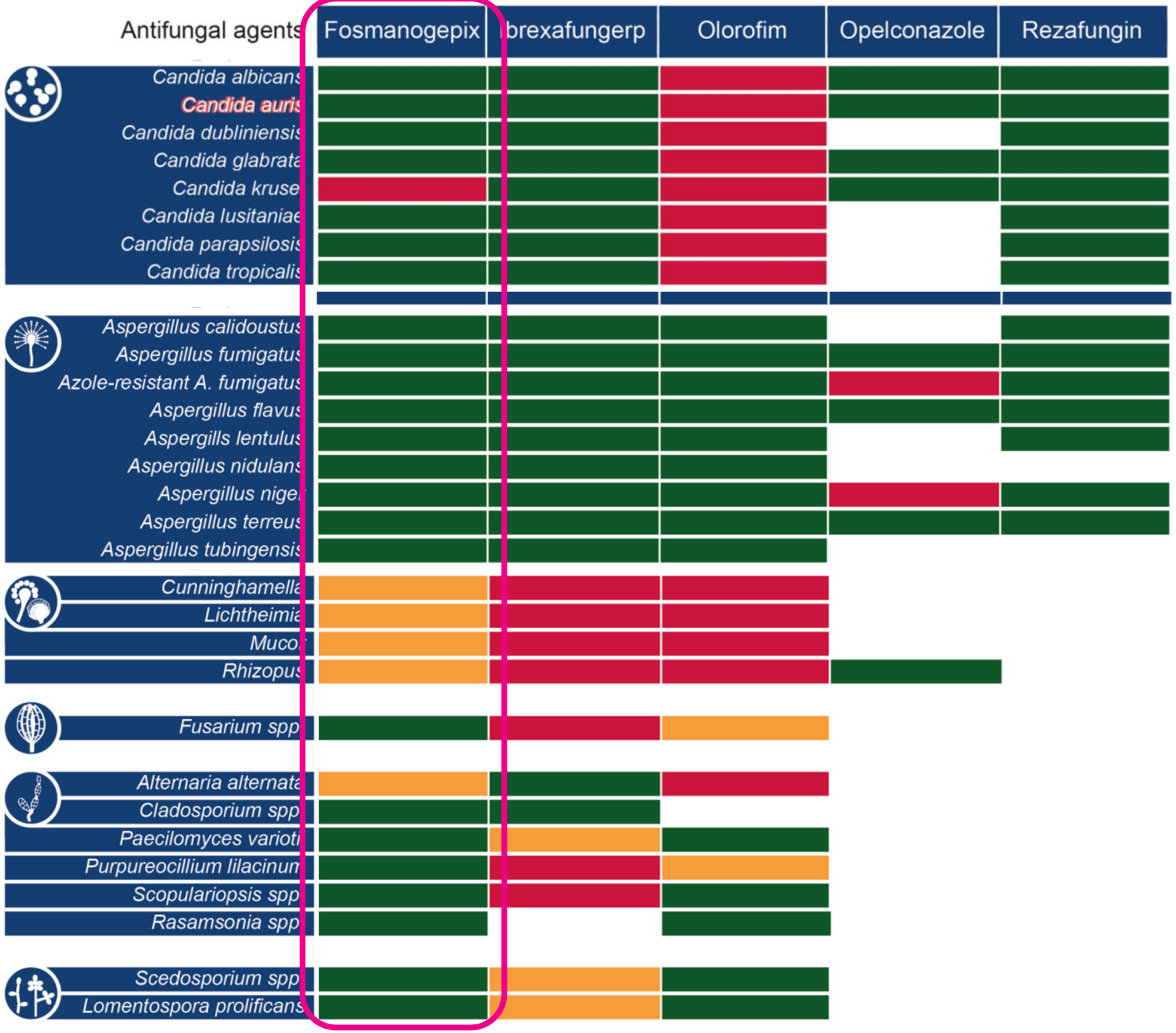
| Future use | Advantages |
|---|---|
| VVC<br>Step-down in candidemia<br>Resistant IPA | Safe<br>Few DDI (CYP3A4!)<br>Oral, outpatient |

FURI trial NCT03059992, ibrexafungerp in refractory fungal disease

MARIO trial NCT05178862, oral step-down following echinocandin in candidemia




Hoenigl, et al. Drugs 2021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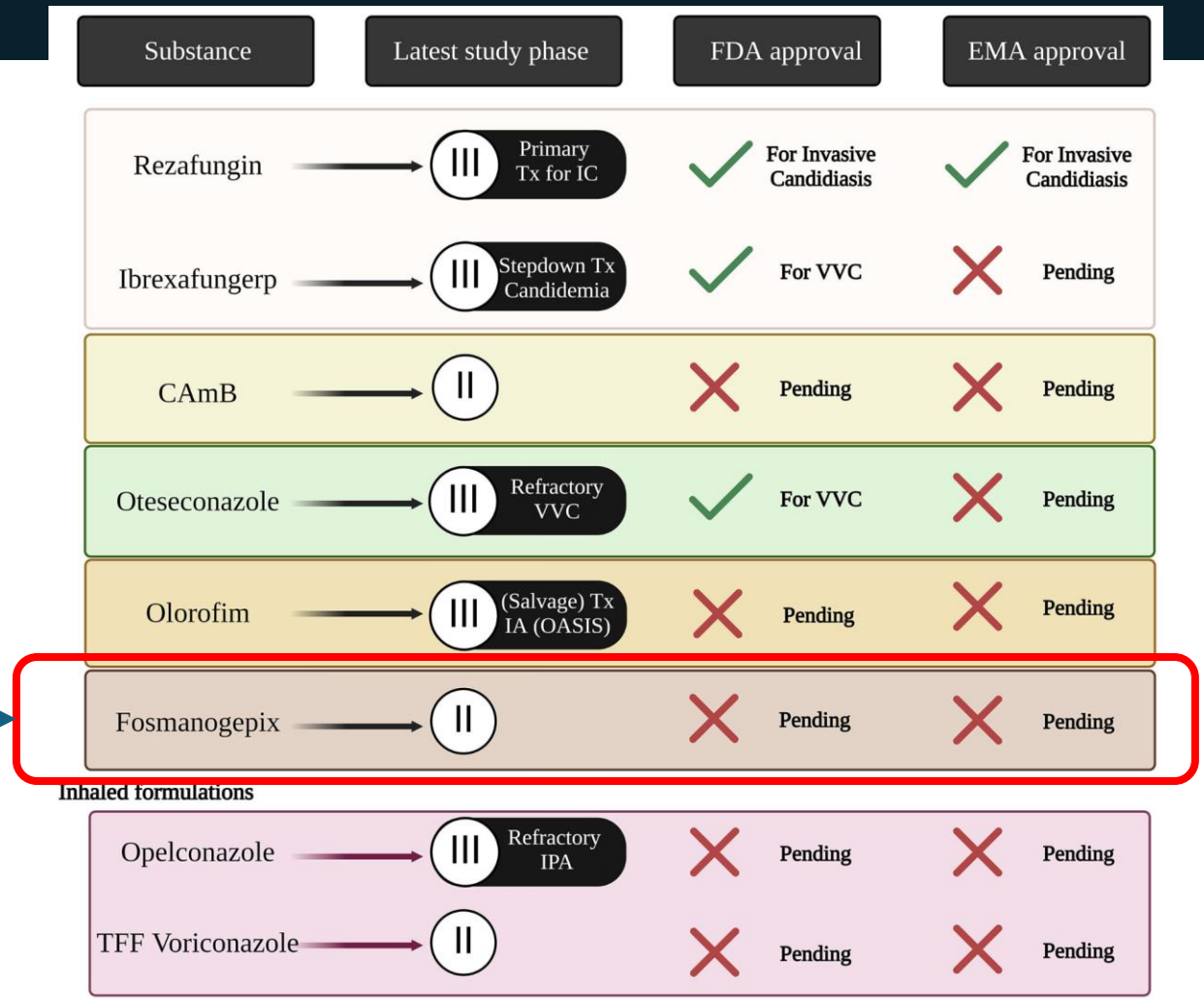
Aspergillus flavus
Aspergills lentulus
Aspergillus nidulans
Aspergillus nige
Aspergillus terreus
Aspergillus tubingensis
Cunninghamella
Lichtheimia
Muco
Rhizopus
Fusarium spp
Alternaria alternata
Cladosporium spp
Paecilomyces varioti
Purpureocillium lilacinum
Scopulariopsis spp
Rasamsonia spp
Scedosporium spp
Lomentospora prolificans

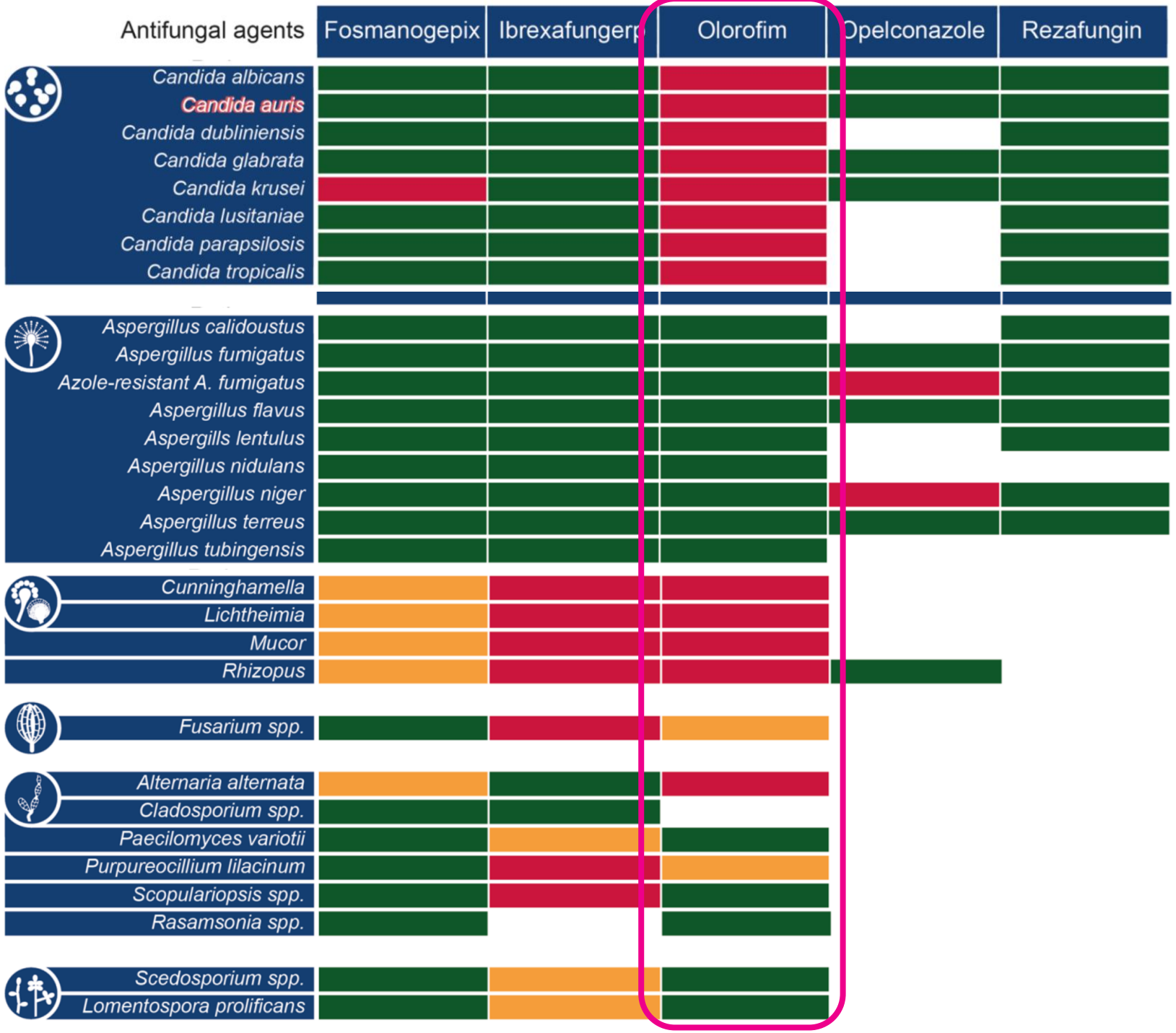
# Future treatment options – Fosmanogepix

| Future use | Advantages |
|---|---|
| Difficult-to-treat IFD<br>*Candida*<br>*Aspergillus* | Safe<br>Sinergy with L-AMB in Mucor |

Phase 1-2 studies for safety

Phase 3 trial in candidemia (iv -> oral) vs. caspo -> fluco is in programme

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Aspergillus nidulans
Aspergillus niger
Aspergillus terreus
Aspergillus tubingensis
Cunninghamella
Lichtheimia
Mucor
Rhizopus
Fusarium spp.
Alternaria alternata
Cladosporium spp.
Paecilomyces variotii
Purpureocillium lilacinum
Scopulariopsis spp.
Rasamsonia spp.
Scedosporium spp.
Lomentospora prolificans

# Future treatment options – Olorofim

| Future use | Advantages |
|---|---|
| Resistant mould infections<br>Endemic mycoses | Anti-biofilm<br>Active if limited options |

No RCT published
FORMULA study results (2023)*
OASIS NCT05101187, phase III trial, IPA, olorofim vs. L-AMB

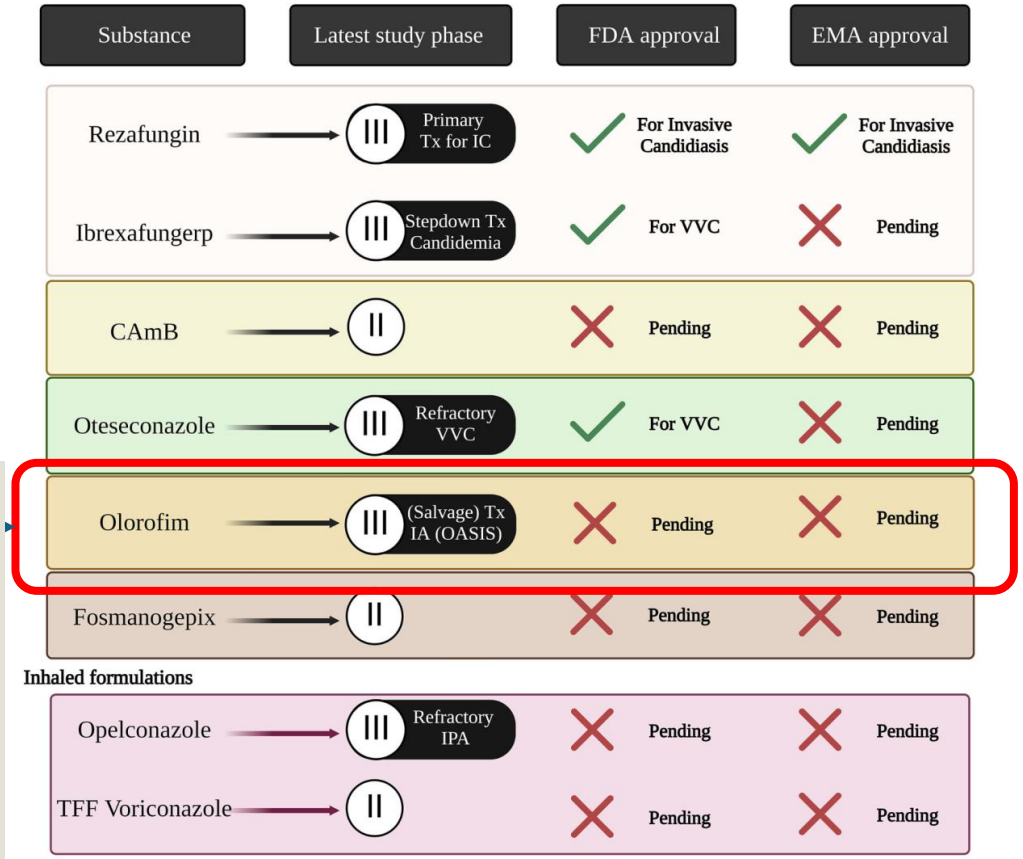
E0547
**Outcomes of IFI due to *Lomentospora prolificans* in 26 pa**
**IIb study of patients with limited or no treatment options (**

06. Fungal infection & disease
06d. Antifungal drugs & treatment (incl pre-clinical studies and clinical tria

M. Slavin [1], J. Maertens [2], O. Morrissey [3], M. Ho [4], J. Schaenman [5], D.L. Paterson [6], M.H. Nguye
[1]Peter Macullum Cancer Centre - Melbourne (Australia), [2]UZ Leuven - Leuven (Belgium), [3]The
(Austria), [5]UCLA - Los Angeles (United States), [6]Singapore - Singapore (Singapore), [7]UPMC -
Manchester (United Kingdom), [10]F2G - Princeton (United States)

- Results from 202 enrolled patients (Maertens TIMM 2023)
  - Overall well tolerated (up to >900days);
  - AESI: elevation of hepatic transaminases: 9.9% of subjects
  - Transaminitis typically within first 12 weeks often managed successfully by Olorofim dose reduction, but required Olorofim discontinuation in 2.5% of subjects

| | Partial/complete response Day 84 | All cause mortality Day 84 |
|---|---|---|
| IA (limited/no Tx options) | 34/101 (33.7%) | 26/101 (25.7%) |
| *Lomentospora prolificans* | 11/26 (42.3%) | 3/26 (11.5%) |
| *Scedosporium* spp. | 5/22 (22.7%) | 2/22 (9.1%) |
| *Scopulariopsis spp.* | 5/6 (83.3%) | 0 |



E0539

# *In vitro* activity of olorofim against global *Aspergillus* spp. isolates

06. Fungal infection & disease

06c. Antifungal susceptibility testing & resistance (incl surveillance, mechanisms)

C. Pinder [1], M. Birch [1], M.C. Arendrup [2], J. Buil [3], P. Verweij [3], J. Guinea [4], D. Law [1].

*[1]F2G Ltd - Manchester (United Kingdom), [2]Statens Serum Institut - Copenhagen (Denmark), [3]Radboud University - Nijmegen (Netherlands), [4]Hospital Gregorio Maranon - Madrid (Spain)*



Table 1. MIC distributions of the most common species of Aspergillus (mg/L).

| Species | N= | 0.002 | 0.004 | 0.008 | 0.015 | 0.03 | 0.06 | 0.12 | 0.25 | 0.5 | 1 | 2 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| *Aspergillus fumigatus* | 4876 | 10 | 54 | 353 | 1594 | 1352 | 1182 | 293 | 34 | 4 | 0 | 0 |
| *Aspergillus niger* | 495 | 3 | 4 | 9 | 71 | 154 | 155 | 82 | 17 | 0 | 0 | 0 |
| *Aspergillus flavus* | 444 | 7 | 13 | 32 | 196 | 137 | 55 | 3 | 1 | 0 | 0 | 0 |
| *Aspergillus terreus* | 384 | 7 | 30 | 102 | 123 | 91 | 28 | 3 | 0 | 0 | 0 | 0 |
| *Aspergillus tubingensis* | 74 | 0 | 0 | 0 | 4 | 21 | 38 | 10 | 1 | 0 | 0 | 0 |
| *Aspergillus nidulans* | 89 | 4 | 13 | 3 | 13 | 20 | 21 | 13 | 2 | 0 | 0 | 0 |
| *Aspergillus calidoustus* | 57 | 0 | 0 | 0 | 1 | 2 | 6 | 11 | 23 | 13 | 1 | 0 |

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E0540

# EUCAST olorofim MICs for 2504 Danish mould and dermatophyte isolates from 2020-2022

06. Fungal infection & disease

06c. Antifungal susceptibility testing & resistance (incl surveillance, mechanisms)

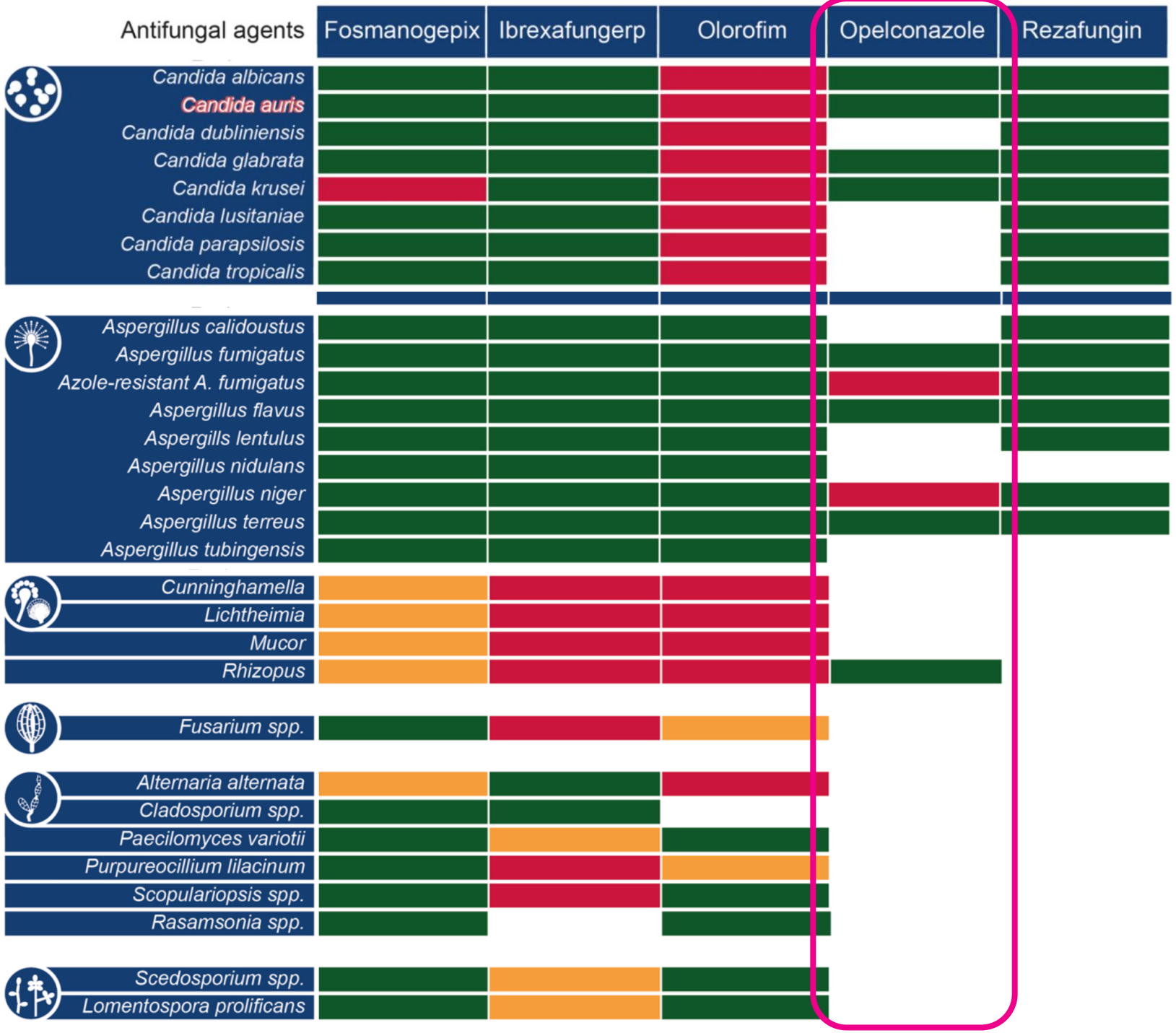
K.M. Joergensen [1], K. Astvad [1], R.K. Hare [1], N. Abou-Chakra [1], M.C. Arendrup [1, 2].

*[1]Unit of Mycology, Statens Serum Institut - Copenhagen (Denmark), [2]Dept Clin Microbiol, Rigshospitalet, Copenhagen University - Copenhagen (Denmark)*

Table 1.

**Table 1.** Olorofim MICs (mg/L) for 2504 moulds obtained 2020-2022. For species with ≥10 isolates, modal MICs are shown in bold, $MIC_{50}$s are in italic, and $MIC_{90}$s are underscored.

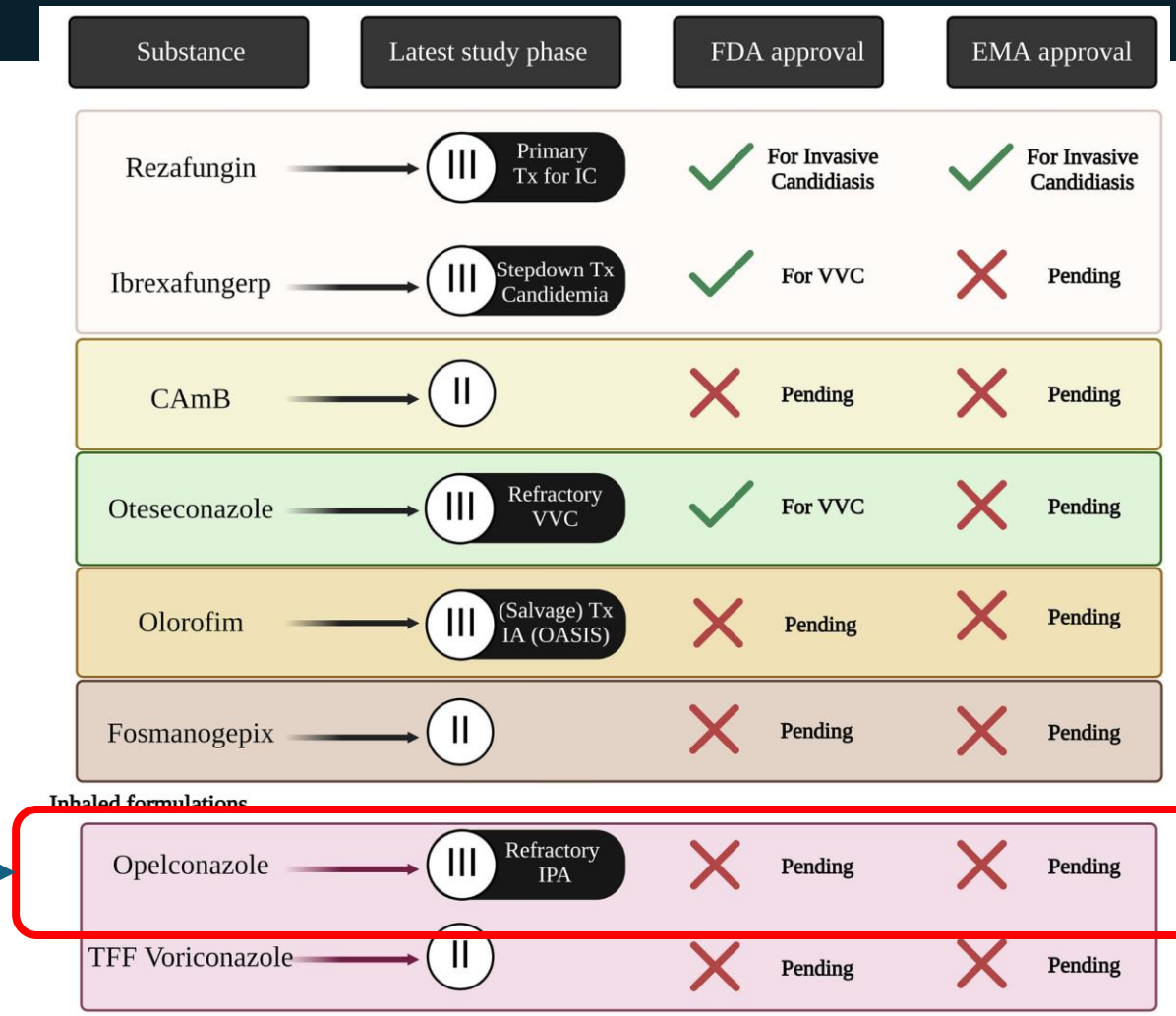
| | N | MIC (mg/L) | | | | | | | | | | WT-UL | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 0.004 | 0.008 | 0.016 | 0.03 | 0.06 | 0.125 | 0.25 | 0.5 | 1 | >1 | 97.5% | 99.5% | 99.9% |
| ***Aspergillus*** | | | | | | | | | | | | | | |
| *A. flavus* complex | 64 | | | 4 | ***34*** | 26 | | | | | | 0.06 | 0.125 | 0.125 |
| *A. fumigatus*[1] | 1894 | | | 16 | 429 | ***1200*** | 240 | 8 | 1 | | | 0.125 | 0.125 | 0.25 |
| *A. nidulans* complex[2] | 30 | | | | | ***19*** | 11 | | | | | 0.125 | 0.125 | 0.125 |
| *A. versicolor* complex[2] | 10 | | 2 | ***5*** | 3 | | | | | | | | | |
| *A. niger* complex | 196 | | | | 3 | 59 | ***113*** | 20 | 1 | | | 0.25 | 0.25 | 0.5 |
| *A. terreus* complex | 54 | | | 10 | ***25*** | 15 | 4 | | | | | 0.125 | 0.125 | 0.25 |
| Other *Aspergillus*[3] | 20 | | | | 3 | 4 | | 2 | 3 | 1 | 7 | | | |
| ***Fusarium*** | | | | | | | | | | | | | | |
| *F. fujikuroi* complex | 6 | | | | 1 | 1 | 1 | 1 | 2 | | | | | |
| *F. oxysporum* complex | 3 | | | | | | | 1 | 2 | | | | | |
| *F. avenaceum* | 1 | | | | | | | | | 1 | | | | |
| *F. solani* complex | 3 | | | | | | | | | 1 | 2 | | | |
| *F. dimerum* | 6 | | | | | | | | | | 6 | | | |
| **Other moulds** | | | | | | | | | | | | | | |
| *Scedosporium apiospermum* | 11 | | | | 4 | *3* | 4 | | | | | | | |
| *Scedosporium* spp. | 3 | | | 1 | | 1 | 1 | | | | | | | |
| Rare moulds, MIC ≤1 mg/L[4] | 29 | | 1 | 1 | 3 | 1 | 8 | 5 | 6 | 4 | | | | |
| Rare moulds, MIC >1 mg/L[5] | 5 | | | | | | | | | | 5 | | | |
| **Dermatophytes** | | | | | | | | | | | | | | |
| *T. rubrum* | 98 | 1 | 15 | ***48*** | 29 | 5 | | | | | | 0.06 | 0.06 | 0.06 |
| *T. indotineae* | 28 | | 3 | ***16*** | 5 | 4 | | | | | | 0.03 | 0.03 | 0.06 |
| *T. interdigitale* | 13 | | 4 | ***6*** | 1 | 2 | | | | | | | | |
| Other *Trichophyton*[6] | 13 | | 1 | 3 | 7 | 2 | | | | | | | | |
| *M. audouinii* | 15 | | | | | 2 | 8 | 2 | 1 | 2 | | 0.25 | 0.25 | 0.5 |
| *M. canis* | 2 | | | | 2 | | | | | | | | | |


Antifungal agents
Fosmanogepix
Ibrexafungerp
Olorofim
Opelconazole
Rezafungin
Candida albicans
Candida auris
Candida dubliniensis
Candida glabrata
Candida krusei
Candida lusitaniae
Candida parapsilosis
Candida tropicalis
Aspergillus calidoustus
Aspergillus fumigatus
Azole-resistant A. fumigatus
Aspergillus flavus
Aspergills lentulus
Aspergillus nidulans
Aspergillus niger
Aspergillus terreus
Aspergillus tubingensis
Cunninghamella
Lichtheimia
Mucor
Rhizopus
Fusarium spp.
Alternaria alternata
Cladosporium spp.
Paecilomyces variotii
Purpureocillium lilacinum
Scopulariopsis spp.
Rasamsonia spp.
Scedosporium spp.
Lomentospora prolificans

# Future treatment options – Opelconazole

| Future use | Advantages |
|---|---|
| Pulmonary aspergillosis<br>Proph. in lung Tx<br>Combination Tx | Low DDI<br>Local lung action |

Phase III trial in refractory IPA + SoC ongoing



Oral AMB, no renal toxicity
Phase 2 on VVC and **CM**
Phase 3 on IPA planned

Future: **CM**, endemic mycoses

Tetrazole
Long half-life
Embryo-fetal toxicity

Future: **rVVC?**

| Substance | Latest study phase | FDA approval | EMA approval |
|---|---|---|---|
| Rezafungin | III Primary Tx for IC | ✓ For Invasive Candidiasis | ✓ For Invasive Candidiasis |
| Ibrexafungerp | III Stepdown Tx Candidemia | ✓ For VVC | ✗ Pending |
| CAmB | II | ✗ Pending | ✗ Pending |
| Oteseconazole | III Refractory VVC | ✓ For VVC | ✗ Pending |
| Olorofim | III (Salvage) Tx IA (OASIS) | ✗ Pending | ✗ Pending |
| Fosmanogepix | II | ✗ Pending | ✗ Pending |
| **Inhaled formulations** | | | |
| Opelconazole | III Refractory IPA | ✗ Pending | ✗ Pending |
| TFF Voriconazole | II | ✗ Pending | ✗ Pending |

Hoenigl, et al. Drugs 2021

# Grazie per l'attenzione

SCUOLA DI SPECIALIZZAZIONE IN MALATTIE INFETTIVE E TROPICALI

PANDORA ID - 24

TIME TO WEBINAR IN INFECTIOUS DISEASES