

CHALLENGING IN COVID 19 TREATMENT ASSOCIATED IFI

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Challenging in COVID 19 treatment associated IFI









ORIGINAL ARTICLE

Occurrence of Invasive Pulmonary Fungal Infections in Patients with Severe COVID-19 Admitted to the ICU

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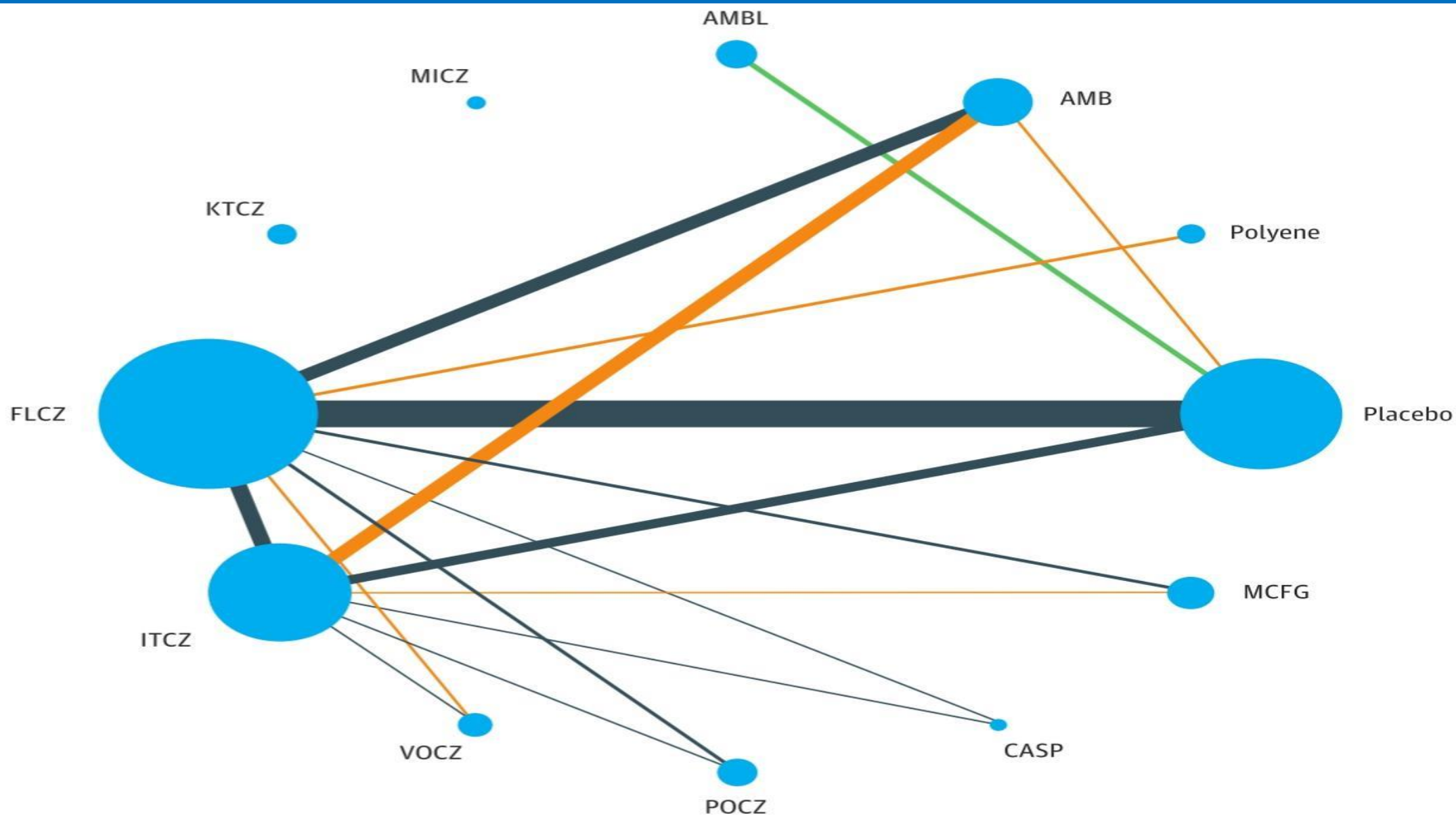
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Risk factors:

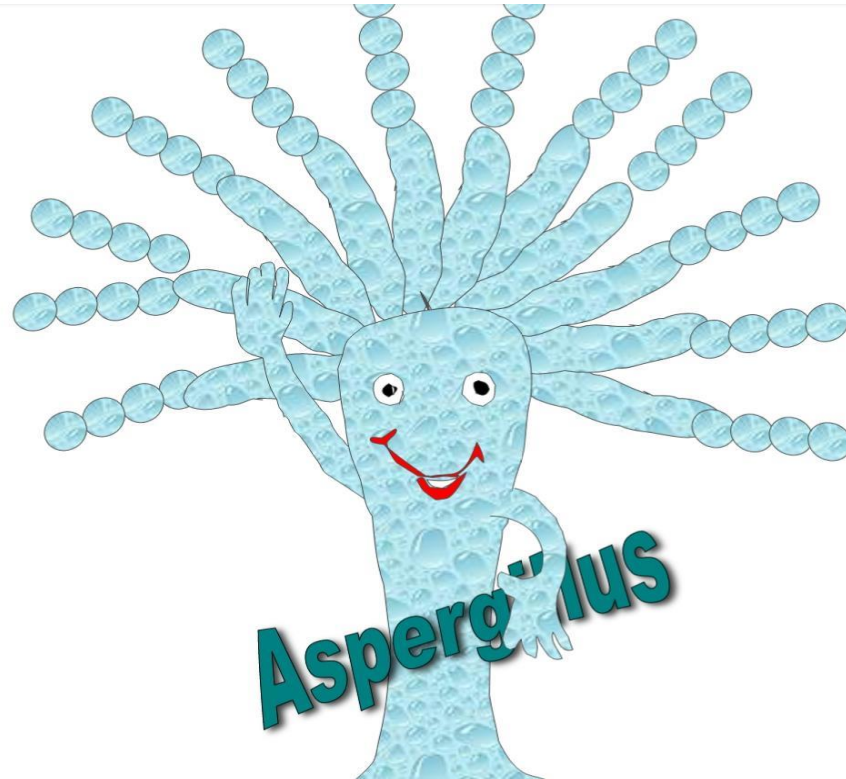
- **Immunosuppression by steroids**
- **Prolonged ICU stay**
- **Voriconazole therapy**
- **Use antibiotics/antifungals**

Table 3: Prevention of rhino-orbito-cerebral mucormycosis in the setting of COVID-19

- Judicious and supervised use of systemic corticosteroids in compliance with the current preferred practice guidelines
 - Judicious and supervised use of tocilizumab in compliance with the current preferred practice guidelines
 - Aggressive monitoring and control of diabetes mellitus
 - Strict aseptic precautions while administering oxygen (sterile water for the humidifier, daily change of the sterilized humidifier and the tubes)
 - Personal and environmental hygiene
 - Betadine mouth gargle (not nasal drops)
 - Barrier mask covering the nose and mouth
 - Consider prophylactic oral Posaconazole in high-risk patients (>3 weeks of mechanical ventilation, >3 weeks of supplemental oxygen, >3 weeks of systemic corticosteroids, uncontrolled diabetes mellitus with or without ketoacidosis, prior history of chronic sinusitis, and co-morbidities with immunosuppression)
-



Invasive Aspergillosis



ECIL-6 recommendations for first-line treatment of invasive aspergillosis

Voriconazole	AI	Daily dose: 2x6 mg/kg on day 1 then 2x4 mg/kg (initiation with oral therapy: C III)
Isavuconazole	AI	As effective as voriconazole and better tolerated
Liposomal amphotericin	B I	Daily dose: 3 mg/kg
Amphotericin B lipid complex	B II	Daily dose: 5 mg/kg
Amphotericin B colloidal dispersion	C I	Not more effective than d-AmB but less nephrotoxic
Caspofungin	C II	
Itraconazole	C III	
Combination vorico + anidulafungin	C I	
Other combinations	C III	

Posaconazole

- Posaconazole is highly active in vitro against *Aspergillus* spp
- A recent phase 3 study comparing posaconazole to voriconazole in the treatment of invasive infection has been presented but has not yet been published
- Posaconazole initially was available only as an oral suspension and required administration in divided doses, 2 times to 4 times per day, and suffered from poor absorption.
- A delayed-release oral tablet and an IV formulation since have been developed substantial improving serum drug levels.
- Posaconazole achieves high levels in peripheral tissues, such as lung, kidneys, liver, and heart, and there are limited data regarding penetration into the CNS

Invasive Aspergillosis

- **Aspergillus fumigatus** resistance is caused most commonly .
- Resistance may develop following **long durations of therapy**, particularly in those with **chronic cavitory disease**, although **de novo resistance** also may be found, particularly in regions using **azoles on agricultural products**

- The management of patients infected with **azole-resistant** infection is :
- **lipid AmB** products and combination therapy with an **azole or echinocandin**

- **Voriconazole** is the treatment of choice in most patients; isavuconazole, **posaconazole**, and **L-AmB** are important alternative agents.
- **Combination** therapy can be used in select patients with more **extensive** infection and in those with significant and **ongoing immunosuppression**.

Mucormycosis

- **Mucorales are intrinsically resistant to :**
- **Fluconazole**
- **Itraconazole**
- **Voriconazole**
- **Echinocandins**
- **Flucytosine**

Journal de Mycologie Médicale

Volume 30, Issue 3, September 2020, 101007

General review

Mucormycosis treatment: Recommendations, latest advances, and perspectives

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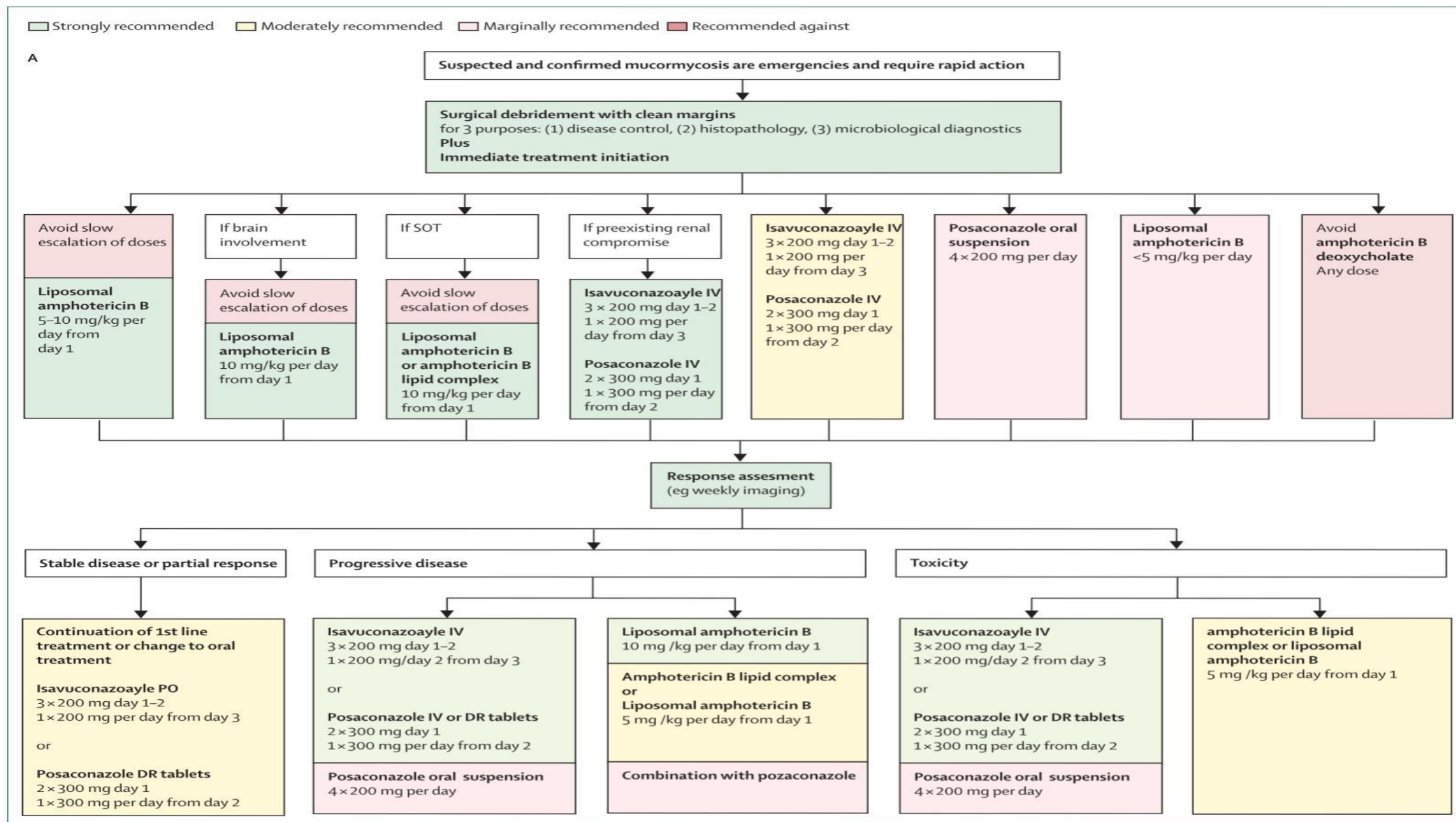


Global guideline for the diagnosis and management of mucormycosis: an initiative of the European Confederation of Medical Mycology in cooperation with the Mycoses Study Group Education and Research Consortium



Oliver A Cornely, Ana Alastruey-Izquierdo, Dorothee Arenz, Sharon C A Chen, Eric Dannaoui, Bruno Hochhegger, Martin Hoenigl, Henrik E Jensen, Katrien Lagrou, Russell E Lewis, Sibylle C Mellinghoff, Mervyn Mer, Zoi D Pana, Danila Seidel, Donald C Sheppard, Roger Wahba, Murat Akova, Alexandre Alanio, Abdullah M S Al-Hatmi, Sevtap Arian-Akdagli, Hamid Badali, Ronen Ben-Ami, Alexandro Bonifaz, Stéphane Bretagne, Elio Castagnola, Methee Chayakulkeeree, Arnaldo L Colombo, Dora E Corzo-León, Lubos Drgona, Andreas H Groll, Jesus Guinea, Claus-Peter Heussel, Ashraf S Ibrahim, Souha S Kanj, Nikolay Klimko, Michaela Lackner, Frederic Lamothe, Fanny Lanternier, Cornelia Lass-Floerl, Dong-Gun Lee, Thomas Lehrnbecher, Badre E Lmimouni, Mihai Mares, Georg Maschmeyer, Jacques F Meis, Joseph Meletiadis, C Orla Morrissey, Marcio Nucci, Rita Oladele, Livio Pagano, Alessandro Pasqualotto, Atul Patel, Zdenek Racil, Malcolm Richardson, Emmanuel Roilides, Markus Ruhnke, Seyedmojtaba Seyedmousavi, Neeraj Sidharthan, Nina Singh, János Sinkó, Anna Skiada, Monica Slavin, Rajeev Soman, Brad Spellberg, William Steinbach, Ban Hock Tan, Andrew J Ullmann, Jörg J Vehreschild, Maria J G T Vehreschild, Thomas J Walsh, P Lewis White, Nathan P Wiederhold, Theoklis Zaoutis, Arunaloake Chakrabarti, for the Mucormycosis ECMM MSG Global Guideline Writing Group





(Figure 5 continues on next page)

ECIL-6 recommendations for salvage and maintenance therapy of mucormycosis.

Management includes: -Antifungal therapy -Control of underlying disease -Surgery	All
Posaconazole	B II
Combination of lipid amphotericin B and caspofungin	B III
Combination of lipid amphotericin B and posaconazole	B III

Review

Therapy of Mucormycosis

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Dimitrios P. Kontoyiannis ^{2,*}**

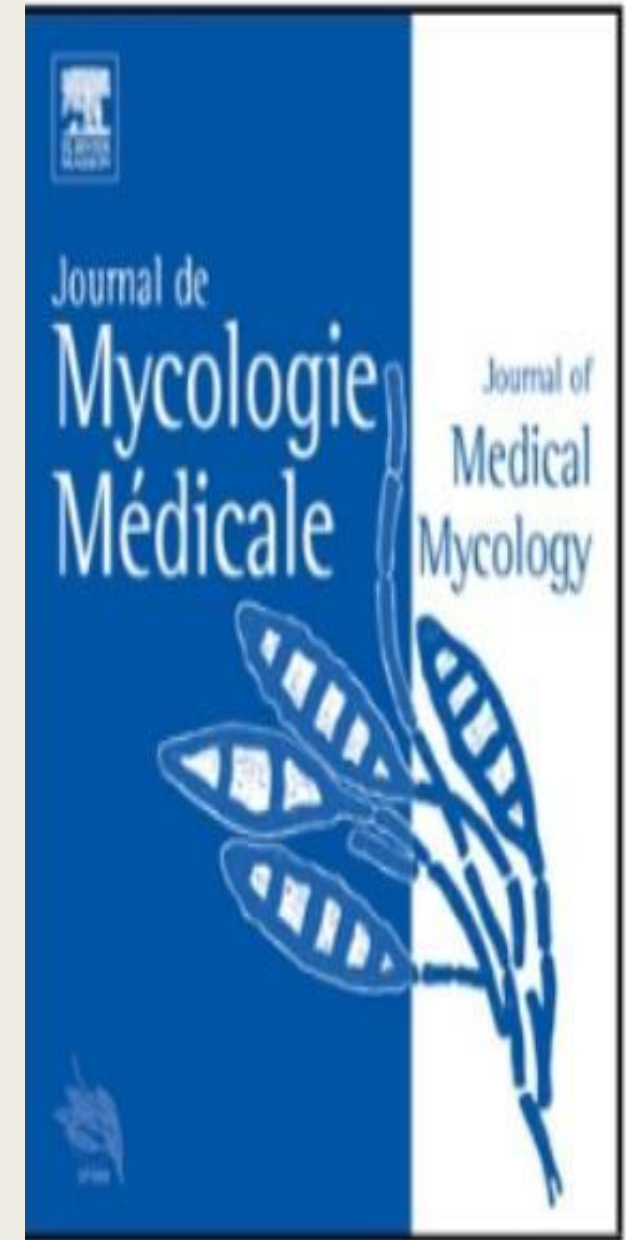
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- Clinical data do not support the use of combination therapy, with the possible **exception of CNS mucormycosis**, where a combination of high-dose LAMB and posaconazole or isavuconazole might be considered.

- **Combination are not currently recommended for first-line therapy** due to lack evidence of their efficacy.
- **Combinations of antifungal agents have been largely tested in vitro. Most combinations were indifferent, except for AmB + caspofungin (CAS), PSZ + CAS and ISZ + CAS which were synergistic**



- **Combination** antifungal therapy is typically used by many physicians in an attempt to maximize treatment of this **devastating** disease, especially in patients with **profound immunosuppression** that cannot be reverted

- Despite a paucity of data, many experts support the use of combination therapy with **L-AmB and posaconazole**, given the potential clinical benefit and the lack of evidence for antagonism between the drugs.
- **Echinocandins** have also been used in combination with AmB despite their lack of activity against Mucorales.
- The clinical experience using combination therapy with **echinocandins and AmB** is limited to small retrospective series and case reports.

Thank You!