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

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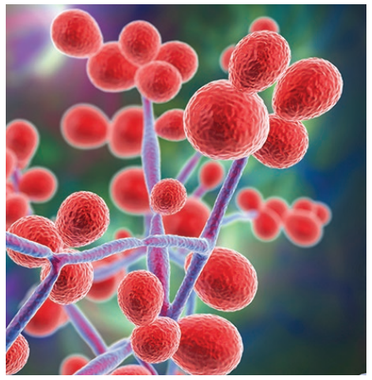
Invasive Candidiasis (IC) Summary

- Over 1,565,000 people diagnosed with IC every year
- *Candida* species are the predominant cause of fungal infections in patients treated in hospital, contributing substantially to morbidity and mortality
- Candidemia and other forms of invasive candidiasis primarily affect patients who are immunocompromised or critically ill
- The rise of difficult-to-treat *Candida* infections is driven by new host factors and antifungal resistance
- Pathogens, such as *Candida auris* and fluconazole-resistant *Candida parapsilosis*, pose serious global health risks, particularly in hospital environments where transmission is easily facilitated
- Susceptibility testing is particularly important in settings with acquired resistance, as the species identification may not provide enough data for selecting appropriate therapy
- This review article provides updated recommendations for managing *Candida* infections

Abbreviations:
ECMM: European Confederation of Medical Mycology
ISHAM: International Society for Human and Animal Mycology
ASM: American Society for Microbiology

Epidemiology

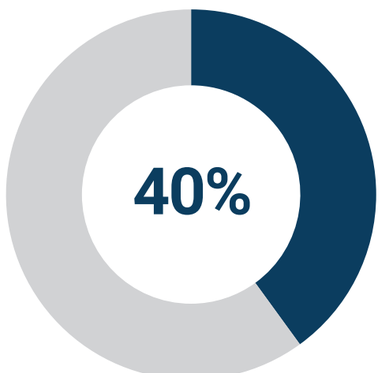
The Rise of Difficult-to-Treat *Candida* Infections



- An increasing number of patients have difficult-to-treat invasive candidiasis due to new, underlying host factors or antifungal resistance, causing increasing health-care use, economic burden, and mortality
- The effectiveness of triazoles for the treatment of candidemia has declined in recent decades because of the increasing prevalence of *Candida* spp. that are intrinsically tolerant to azoles, such as *C. glabrata,* and of species resistant to these drugs by intrinsic or acquired mechanisms

- New targeted biologics drugs such as IL-17 inhibitors predispose for *Candida* infections
- Knowledge of local epidemiology should be taken into account as species distribution and prevalence of acquired resistance differ notably

Intra-abdominal Candidiasis (IAC)



- Intra-abdominal candidiasis occurs in approximately 40% of patients with repeated gastrointestinal surgery, gastroduodenal perforation and necrotizing pancreatitis
- It is associated with increased mortality rates
- <15% of patients with IAC have blood cultures positive for *Candida* spp

Please see accompanying Prescribing Information for REZZAYO® (rezafungin for injection).

Strong Guideline Recommendations

Echinocandins: First Line for Invasive Candidiasis

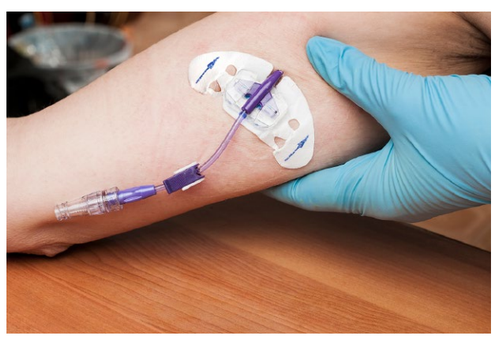
First Line Treatment: Optimal treatment pathway for candidemia without organ involvement in adults*

- Echinocandins, including rezafungin†, are the recommended first-line treatment for candidemia and all forms of invasive candidiasis except for CNS and ocular infections
- Switch to oral azole only if:
  - Hemo-dynamically stable
  - Documented clearance of *Candida* from the bloodstream
  - Non-neutropenic
  - Source control performed
  - Able to tolerate oral azoles
  - Susceptibility confirmed to the selected azole
- Echinocandins are first line for any intra-abdominal candidiasis (other than peritoneal-dialysis associated fungal peritonitis) including abdominal abscess

Echinocandins	**Strongly Recommended**
Fluconazole, voriconazole, liposomal amphotericin B	**Moderately Recommended**
Amphotericin B lipid complex, isavuconazole	**Marginally Recommended**

*Adapted from Figure 2

Catheter-Related Bloodstream Infections



- Central venous catheters (CVC) are important risk factors for candidemia
- The catheter is often involved in the infection either as source or after becoming colonized
- CVC removal in patients with candidemia is strongly recommended as early as possible (<48-72 h)

Please see full Indication and Important Safety Information for REZZAYO® on back cover.

New global candidiasis guidance recommends *REZZAYO*®

Rezafungin in the Guideline

Echinocandins, including rezafungin†, are the recommended first-line treatment for candidemia and all forms of invasive candidiasis except for CNS and ocular infections due to their broad activity and safety profile.

- The rezafungin PK characteristics with low clearance, long half-life and a once weekly front-loaded dosing regimen, may be advantageous in treating species with elevated MICs‡
- For the new long-acting echinocandin rezafungin, a population PK analysis indicates that rezafungin does not need dose adjustment in obese, elderly or renally impaired patients
- A Phase 1 hepatic impairment study identified that there is no requirement to dose adjust for patients with hepatic impairment

‡In vitro activity does not necessarily correlate to clinical efficacy.

†INDICATION AND USAGE

REZZAYO® (rezafungin for injection) is an echinocandin antifungal indicated in patients 18 years of age or older who have limited or no alternative options for the treatment of candidemia and invasive candidiasis. Approval of this indication is based on limited clinical safety and efficacy data.

Limitations of Use

REZZAYO® has not been studied in patients with endocarditis, osteomyelitis, and meningitis due to *Candida*.

IMPORTANT SAFETY INFORMATION

Contraindications

REZZAYO® is contraindicated in patients with known hypersensitivity to rezafungin or other echinocandins.

Warnings and Precautions

- Infusion-related Reactions: REZZAYO® may cause infusion-related reactions, including flushing, sensation of warmth, urticaria, nausea, or chest tightness. If these reactions occur, slow or pause the infusion.
- Photosensitivity: REZZAYO® may cause photosensitivity. Advise patients to use protection from sun exposure and other sources of UV radiation.
- Hepatic Adverse Reactions: Abnormalities in liver tests have been seen in clinical trial patients treated with REZZAYO®. Monitor patients who develop abnormal liver tests and evaluate patients for their risk/benefit of continuing REZZAYO® therapy.

Adverse Reactions

Most common adverse reactions (incidence ≥ 5%) are hypokalemia, pyrexia, diarrhea, anemia, vomiting, nausea, hypomagnesemia, abdominal pain, constipation, and hypophosphatemia.

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Please see accompanying Prescribing Information for REZZAYO® (rezafungin for injection).

REZZAYO™ (rezafungin for injection)