Invasive fungal infections (IFIs) remain a leading cause of morbidity and mortality in immunocompromised patients. Among those, patients with hematological malignancies and those who have undergone solid organ or allogeneic hematopoietic stem cell transplantation are at particularly high risk. Species of *Candida* and *Aspergillus* remain the most common causes of IFIs; however, other yeasts and filamentous fungi are emerging as significant pathogens. The sensitive and specific diagnosis remains difficult in many cases and early initiation of treatment is mandatory to improve survival. Although major improvements have been made, it often remains difficult to obtain diagnosis in neutropenic patients and treatment of IFIs in this high-risk population remains challenging. A growing armamentarium of novel antifungal agents has been approved in recent years. ‘Old fashioned’ amphotericin B deoxycholate (d-AMB) has been replaced with lipid formulations and new-generation triazoles, as well as novel class echinocandins, which finally offer opportunities to improve prognosis with the convenient side-effect of better tolerability. Clinical decision-making depends on several guidelines, published studies and not least on economic considerations. Future approaches should be directed towards enhanced diagnostic methods and, thus, allow for timely and effective tailor-made use of antifungals.

**Keywords:** antifungal treatment • aspergillus • candida • fungal infection • immunocompromised • mucormycosis
the outcome [10]. Different treatment approaches have been designed depending on individual risk profiles. Empiric or pre-emptive antifungal therapy is started even before IFI is defined as the proven infection subject to EORTC/MSG criteria. If the pathogen is clearly identified, targeted antifungal therapy is administered. Along with improved diagnostic tools and better supportive care, mortality rates linked to fungal infection have been reduced [11].

The current review summarizes recent developments in the epidemiology, diagnosis and treatment of invasive fungal infections with a focus on *Candida*, *Aspergillus* and *Mucormycosis*.

**Risk factors & epidemiology**

In the past decades, IFIs were primarily caused by *Candida* spp. However, several more recent clinical analyses and autopsy studies revealed a significant change in epidemiology and demonstrated mold infections to be the major cause of IFIs [1,2,5–8,11–16]. Invasive aspergillosis (IA) remains the main obstacle to overcome, especially for patients undergoing allogeneic HSCT. In this setting, fluconazole is used liberally for primary prophylaxis, probably resulting in a shift towards mold infections [13].

The number of *Aspergillus* species causing IFIs may be expanding. When clinical disease in the last decade in 90% of cases was secondary to *A. fumigatus*, a large report from 19 healthcare centers in the USA revealed *A. flavus*, *A. terreus*, *A. niger* and *Aspergillus versicolor* (19, 16, 8 and 1%, respectively) to be the causative agents besides *A. fumigatus* (56%) [17]. Regional distinctions in epidemiology may occur, as shown in a retrospective analysis where *A. terreus* was shown to be endemic in Tyrol, Austria [18]. Being aware of those specifics is crucial for the correct choice of antifungal treatment, as for instance *A. terreus* is resistant against amphotericin B deoxycholate (d-AMB).

The overall incidence of IA in patients with hematological malignancies varies between 0.3 and 15%, depending on the underlying disease [1,2,5–8,11]. Tremendous case fatality rates up to 87% are reported, especially for patients following allogeneic HSCT [7,19]. Risk factors for IA include prolonged and severe neutropenia, steroid therapy, HSCT, SOT, chronic granulomatous disease and advanced AIDS [7,18–23]. Recently, other opportunistic mold infections – *Fusarium* spp. and zygomycetes – have emerged. This is of particular interest as mucormycetes are not susceptible to voriconazole, the current gold standard for invasive mold infections [24,25]. Other fungal pathogens remain rare.

Yeast infections are less common than mold infections and *Candida* is still the predominant pathogen. Although *Candida albicans* is the most common cause of candidemia, there has been increased isolation of non-albicans species of *Candida* in recent years [26–30]. In a large multicenter study conducted in the USA, 46% represented *C. albicans* and 54% of bloodstream isolates represented non-albicans *Candida* spp. [29]. Among the latter were *Candida glabrata*, *Candida parapsilosis*, *Candida tropicalis* and *Candida krusei* (26%, 16, 8 and 3%, respectively). Other studies have shown a similar order of frequency although the incidence of each species varies in different patient populations and geographic regions [30]. On multivariate analysis, fluconazole prophylaxis was a risk factor for both *C. glabrata* and *C. krusei* candidemia, neutropenia was a risk factor for all candidemias, and central venous catheter (CVC)-related infection was a risk factor for *C. parapsilosis* candidemia [31,32]. It is postulated that the widespread fluconazole exposure causes selective pressure towards rising isolation of non-*C. albicans* species [33,34]. Knowing the prevalence of the non-*C. albicans* species is important because susceptibility to antifungal agents varies among the species. As an example, all isolates of *C. krusei* are fluconazole resistant and a variable proportion of *C. glabrata* are fluconazole resistant.

Patients who are immunocompromised and those in an intensive care unit (ICU) are most at risk for the development of candidemia. Surgical units, especially those caring for trauma and burn patients, and neonatal units have the highest rates of *Candida* infections [35]. In immunocompromised patients, neutropenia is common and most stem cell/solid-organ recipients are also receiving glucocorticoids following transplantation. Other risk factors include broad-spectrum antibiotics and CVCs [26–28]. Colonization with *Candida* species was also shown to be an independent predictor of candidemia [36]. In summary, an impaired immune status as well as colonization with fungal pathogens, age, class of chemotherapy (increased risk for cytarabine) and the use of novel therapeutics such as monoclonal antibodies increase the risk for IFIs [37–40]. The widespread use of fluconazole in prophylaxis has increased the incidence of molds and in yeast infections, the epidemiology has shifted towards an increased isolation of non-*C. albicans* species.

**Diagnosis of invasive fungal infections**

Timely diagnosis of IFIs is indispensable for successful antifungal treatment. Laboratory evaluation is mainly based on culture-based diagnosis, direct microscopic detection or serologic reactions of fungal metabolites or antigens. For mold infections, major advances have been achieved in the development of diagnostic adjuncts, such as BG or GM [41]. The latter is a major constituent of *Aspergillus* cell walls and is released during growth of hyphae. Early detection
of serum GM by sandwich ELISA has been explored by several groups as a diagnostic test for IA. Other techniques for the detection of this antigen are not sufficiently sensitive for diagnostic use [42]. The GM assay was shown to have the potential to detect antigenemia before the presence of clinical signs, positive cultures or an abnormal chest x-ray in patients at risk for IA. However, this method showed several inadequacies regarding sensitivity and specificity. Thus, active antibiotic treatment with piperacillin/tazobactam or former exposure to systemic antifungals may cause false-positive results for GM whereas a recent meta-analysis found an overall sensitivity of 71% and a specificity of 89% in surveillance of proven IFI according to EORTC/MSG criteria [43–46]. False-positive results may also be seen with infections with organisms that share crossreacting antigens, including penicillium species and Histoplasma capsulatum, and are more likely to occur during the first 100 days following HSCT and in patients with chronic gastrointestinal graft-versus-host disease [47–49]. Furthermore, it was suggested that GM performed better in patients with hematological malignancies or recipients of HSCT compared with its lower performance in SOT recipients [45]. This may be related to the higher incidence of IA in patients with hematologic cancers and because of inadequate number of SOT patients included in this analysis. However, a negative GM assay seems to be helpful in excluding IA in patients with hematologic malignancies. Large randomized studies are warranted to finally define the role of the serum GM antigen assay in IFI diagnosis.

β-D-glucan is a cell wall component of several fungi. The test is not specific for Aspergillus, unlike the GM assay. Sensitivity ranges from 55 to 95% and the specificity ranges from 77 to 96% [50–57]. Different assays, patient populations and study design may be the cause of this variability. The assay, however, appears to be particularly useful in excluding IFI since the negative predictive value was 100% in two studies [52,53]. In one study, in 95 patients with acute leukemia, the time interval between the onset of fever as the first sign of IFI and a positive BG with acute leukemia, the time interval between the shown interaction of anticoagulants with PCR-techniques has been shown [59]. However, high sensitivity of PCR-based testing was demonstrated in four subsequent studies [60–62]. A negative predictive power of PCR for IA has also been postulated in two analyses [63,64]. However, prospective, multicenter studies are lacking.

In summary, detection of aspergillus in cultures and/or by histologic examination is still essential for a diagnosis of definite IA as clinical experience with GM antigen testing, PCR and the BG assay is limited [48,65].

**Treatment of infection**

As shown for candidemia and mucormycosis, timely initiation of antifungal treatment is mandatory for improving the outcome [6,66]. Different treatment approaches have been designed depending on individual risk profiles. Empiric or pre-emptive antifungal therapy is started when IFI does not meet the criteria of proven infection subject to EORTC/MSG criteria. If the pathogen is clearly identified, targeted antifungal therapy is administered. To improve the comparability in efficacy of several antifungals in studies, IFIs are classified as possible, probable and proven infections [46].

In cases of failure in antifungal treatment, salvage therapy is initiated. Failure of treatment is defined as deterioration of infection or lack of improvement 7 days after antifungals in therapeutic dosing have been initiated. Clinical signs are also incorporated in assessment of effectiveness as laboratory parameters (PCR, GM and C-reactive protein) and histological or cultural findings.

- **Targeted antifungal therapy**
  - **Candidemia**
    - **Azoles**
      For several years, fluconazole has been the gold standard for the treatment of invasive candidemia in non-neutropenic patients [67–69]. Two large, randomized, multicenter trials showed equivalent efficacy of fluconazole to d-AMB in non-neutropenic hosts [67,68]. Overall response rates for fluconazole and amphotericin B were similar at 57 and 62%, and 66 and 64% of cases, respectively. Side effects, however, were significantly fewer in the fluconazole than in the d-AMB group. Fluconazole got its approval in 1990 and has an excellent safety profile. Although being available in oral formulation, treatment of IFIs is initiated intravenously [70].

      Based on MIC data, voriconazole showed better *in vitro* activity against *Candida* spp. compared with fluconazole [71]. In cases of renal failure, its clinical use may be limited by accumulation of the intravenous carrier and despite similar clinical effectiveness, costs are higher than with fluconazole. In non-neutropenic patients, voriconazole was better tolerated and demonstrated similar response rates compared with d-AMB followed by fluconazole [72]. It should be reserved to non-neutropenic patients with refractory disease or resistant *Candida* spp. [73].
Data for itraconazole in invasive candidiasis are limited and one study comparing fluconazole with itraconazole in non-neutropenic patients was discontinued due to only one patient reaching the primary end point [74].

Posaconazole is a novelazole that is available exclusively as an oral suspension. It is approved for use as a prophylactic agent for fungal infections in stem cell transplant recipients with graft-versus-host disease and in patients with prolonged neutropenia due to chemotherapy for hematologic malignancies. It is also approved for oral, but not for systemic candidiasis. To date, there are no sufficient data for posaconazole treatment in invasive candidiasis.

Azoles interact with multiple different cytochrome P450 enzymes; alternative antifungal agents, such as echinocandins, may be preferred if patients have comedications that utilize P450 pathways.

Echinocandins
Echinocandins, such as caspofungin, anidulafungin and micafungin, are noncompetitive inhibitors of the synthesis of BG, which is an integral component of the fungal cell wall [75]. The echinocandins are active in vitro against almost all species of Candida and have a favorable toxicity profile with excellent activity against most Candida species. Thus, they are approved for the treatment of candidemia and other forms of invasive candidiasis. In case of infection with C. glabrata or C. krusei, echinocandins are preferred over azoles [75]. One disadvantage is they must be administered intravenously because they are not well absorbed orally.

As stated in the Infectious Disease Society of America (IDSA) guidelines, the decision whether to choose fluconazole versus an echinocandin mainly depends on whether a patient is neutropenic or non-neutropenic. An echinocandin is favored if the patient has moderately severe-to-severe illness, has had prior azole treatment or prophylaxis (A-III), or the isolate is known to be C. glabrata or C. krusei (B-III). Fluconazole is preferred in patients who are less critically ill and who have no recent azole exposure (A-III) [76].

Polyenes
For the last few decades, d-AMB was the standard drug for the treatment of candidiasis showing good in vitro activity against most species of Candida, except for Candida lusitaniae. Its nephrotoxicity has led to the development of various lipid-based derivatives, including liposomal amphotericin B (LAMB) and amphotericin B lipid complex (ABLC). Due to more frequent infusion-related reactions, the use of amphotericin B colloidal dispersion (ABCD) is limited. On the one hand, they have less toxicity, on the other hand they are significantly more expensive than amphotericin deoxycholate.

AGIHO/ECIL/IDSA recommendations
For the treatment of invasive candidemia in neutropenic patients, current international guidelines recommend echinocandins, fluconazole, amphotericin B formulations and voriconazole in various levels (Table 1).

The IDSA recommends an echinocandin (caspofungin (A-II), micafungin (A-II) or anidulafungin (B-III), as well as amphotericin B (A-II) or fluconazole (B-III). The latter should be reserved as an alternative drug for patients not having formerly received treatment with anazole. Mold-active voriconazole treatment is suggested for coverage of coexistent mold infections with B-III level of evidence [79].

The European Conference of Infections in Leukemia (ECIL), however, recommends echinocandins in a B-II level as a consequence of lacking controlled randomized studies. The same evidence level is assigned to lipid formulations of amphotericin B and voriconazole, whereas fluconazole is only rated with a C-III recommendation [76].

The Infectious Diseases Working Party (AGIHO) of the German Society of Haematology and Oncology (DGHO) gave A-I recommendation to LAMB, echinocandins (micafungin, anidulafungin and caspofungin), fluconazole and voriconazole, whereas itraconazole and posaconazole got C-III due to lacking data in this setting. In addition, avoidance of amphotericin B is clearly recommended (E-I) due to its nephrotoxicity [74]. Antifungal combination therapies are generally not recommended due to lacking data in cancer patients.

Removal of CVCs is still discussed controversially but is advised by AGIHO with B-II and by IDSA with B-III levels of evidence.

Aspergillosis
Azoles
In 2002, voriconazole became the new gold standard in the treatment of IA as it proved superior over amphotericin B. After 3 months, successful outcomes were observed in 52.8% of patients in the voriconazole group (complete responses [CR] in 20.8% and partial responses [PR] in 31.9%) and 31.6% of those in the amphotericin B group (CR in 16.5% and PR in 15.0%); the overall survival rate at this time point was 70.8% in the voriconazole group and 57.9% in the amphotericin B group [76]. The improved efficacy compared with conventional antifungals was also demonstrated in several retrospective analyses in patients with hematological malignancies and in allogeneic transplantation [77,78].
The drug has a favorable safety profile, but its use may be limited by several drug interactions caused by cytochrome P450 metabolism. Reversible complication in terms of blurred vision occurs in up to 40% of patients.

Posaconazole is an oral suspension that is also efficacious in mucormycosis, which is clinically primarily indistinguishable from IA. In one retrospective analysis, posaconazole treatment showed a response rate of 42 versus 26% compared with a cohort receiving antifungal standard treatment [79]. It also revealed a significantly better response rate in salvage therapy compared with high-dose LAMB (≥7.5 mg/kg) ± caspofungin [80]. Posaconazole is a well-tolerated drug, but as metabolism utilizes the cytochrome P450 pathway, co-medications have to be considered carefully.

Itraconazole is another azole available in oral but also intravenous formulation, whereas the latter is limited by its potential nephrotoxicity and multiple drug interactions. Furthermore, implementation in antifungal therapy is narrowed by intolerability in approximately one-third of patients, as shown in a noncomparative study with a limited number of patients. Response rate, however, was at least 48% [81].

**Echinocandins**

Caspofungin is approved for the treatment of IA in patients who are intolerant or refractory to standard therapy [82].

In a compassionate salvage treatment trial for proven or probable IA, caspofungin was administered to patients who were intolerant or refractory to standard therapy [82]. The overall response rate was 45%. The drug is well-tolerated and has few interactions [83]. It is used for salvage therapy, often in combination [84]. Another role for caspofungin may be in the treatment of aspergilllusterreus infection, which is highly resistant to amphotericin B [85].

Micafungin shares a similar spectrum of in vitro activity against *C. albicans* and non-*albicans* species of *Candida* and *Aspergillus* species [86]. It has been investigated mostly in a salvage therapy setting and proved efficacy in approximately 36% [87].

Anidulafungin is effective against aspergillus in vitro and in animal models, but clinical data are still limited [88].

**Polyenes**

Until 2000, amphotericin B was the gold standard for the treatment of IA. Its nephrotoxicity paved the way for the development of lipid formulations such as amphotericin B or ABLC. Several clinical studies in patients with hematological malignancies showed an efficacy of 40–70% in the treatment of IA [89-93]. ABLC was suggested to be more toxic.

**Azirole**

Voriconazole is another azole available in oral but also intravenous formulation, whereas the latter is limited by its potential nephrotoxicity and multiple drug interactions. Furthermore, implementation in antifungal therapy is narrowed by intolerability in approximately one-third of patients, as shown in a noncomparative study with a limited number of patients. Response rate, however, was at least 48% [81].

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AGIHO/ECIL/IDSA recommendations

Recommendations are detailed in Table 2. In all current guidelines, voriconazole is recommended as the first choice for treatment of IA [73,93-96]. If clinically justified, a switch to oral treatment is possible. LAMB is well recommended as an alternate option, although with different recommendation levels from A-I (IDSA) to A-II in AGIHO guidelines and B-I in ECIL-3 guidelines with a dosage from 3–5 mg/kg.

However, ABLC got level B-II recommendation in ECIL-3 guidelines at a dosage of 5 mg/kg. It is recommended by AGIHO to avoid treatment with D-AMB

<table>
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<th>Table 1. Recommendations and levels of evidence of IDSA, ECIL and AGIHO for the treatment of invasive candidemia in patients with hematological/oncological malignancies.</th>
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<tr>
<td><strong>Antifungal drug/class</strong></td>
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<tr>
<td><strong>Echinocandins</strong></td>
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<tr>
<td>Caspofungin</td>
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<td>Micafungin</td>
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<td><strong>Polyenes</strong></td>
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<td>Voriconazole</td>
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<td>Fluconazole</td>
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<td>Posaconazole</td>
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<td>Removal of CVC</td>
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†In case of coexisting mold infection.

Strength of recommendation: A: Good evidence to support a recommendation for use. B: Moderate evidence to support a recommendation for use. C: Poor evidence to support a recommendation for use. D: Moderate evidence to support a recommendation against use. E: Good evidence to support a recommendation against use.

Quality of evidence: I: Evidence from at least one properly randomized, controlled trial. II: Evidence from at least one well-designed clinical trial without randomization, from cohort or case–control analytic studies (preferably from more than one center), from multiple time series, or from dramatic results of uncontrolled experiments. III: Evidence from opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

AGIHO: Arbeitsgemeinschaft Infektionstherapie in der Hämatologie/Onkologie der DGHO (Deutsche Gesellschaft für Hämatologie und Onkologie); CVC: Central venous catheter; ECIL: European Conference on Infections in Leukemia; IDSA: Infectious Disease Society of America.
Table 2. Recommendations and levels of evidence of IDSA, ECIL and AGIHO for the front-line treatment of invasive aspergillosis in patients with hematological/oncological malignancies.

<table>
<thead>
<tr>
<th>Antifungal drug/class</th>
<th>AGIHO</th>
<th>IDSA</th>
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<td>Echinocandins</td>
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<tr>
<td>Caspofungin</td>
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<td>C-II</td>
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<td>Anidulafungin</td>
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<td>Polyenes</td>
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<td>IAmpho</td>
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<td>Voriconazole</td>
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<td>Posaconazole</td>
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<td>Combination therapy</td>
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<td>D-III</td>
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<td>Surgery</td>
<td>B-III</td>
<td>B-III</td>
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Strength of recommendation. A: Good evidence to support a recommendation for use. B: Moderate evidence to support a recommendation for use. C: Poor evidence to support a recommendation for use. D: Moderate evidence to support a recommendation against use. E: Good evidence to support a recommendation against use.

Quality of evidence. I. Evidence from at least one properly randomized, controlled trial. II: Evidence from at least one well-designed clinical trial without randomization, from cohort or case–control analytic studies (preferably from more than one center), from multiple time series, or from dramatic results of uncontrolled experiments. III: Evidence from opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

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due to its nephrotoxicity (E-I) and the drug is no longer graded anymore in any guideline. In absence of data for the first-line treatment of IA, posaconazole has not been graded by any guideline. As there are no studies comparing intravenous itraconazole with polyenes or azoles in IA, this substance is only recommended when other formulations are not tolerated (B-III, AGIHO, C-III, ECIL-3).

Only limited experiences are available for treatment of IA with caspofungin. Therefore, this therapy is recommended in a C-II level by ECIL-3 and only as salvage therapy by AGIHO (A-II). As data on micafungin treatment to date are limited, the drug is not graded by ECIL-3, but is recommended with a C-III level in AGIHO guidelines and is indicated for salvage therapy in all recent guidelines. As of yet, data on treatment with anidulafungin are very limited.

Primary combination therapy is recommended at level B-III by AGIHO and IDSA, and C-III by ECIL-3 guidelines for selected cases. For singular lesions, namely affecting great vessels or causing hemoptysis, surgical resection is recommended if it is feasible (A-II, AGIHO).

Granulocyte colony-stimulation growth factors have been studied in several uncontrolled studies and failed to prove significant improvement in outcome of patients with IA [97,98]. However, IDSA guidelines mentioned growth factors as a subsidiary option for neutropenic patients (B-III), as well as granulocyte transfusions, in case of available granulocytes from a healthy donor [97-99].

Mucormycosis

Invasive infections with mucormycota (new: glomerulamycomata) remain rare but are increasingly noted [100,101]. Case fatality rates reach up to 90% and timely initiation of adequate antifungal therapy is indispensable [102]. Other than in IA, radical surgical debridement should be performed in patients in the condition for such a procedure, as it was shown that additional surgery improves the case fatality rate compared with antifungal treatment alone [100,101]. Therefore, AGIHO guidelines recommend surgical intervention in B-III level by IDSA and C-III by ECIL-3 [74,97,103]. Retrospective analyses have shown high cumulative doses of amphotericin B to be related to improved prognosis [100,104]. ABLC was shown to cause responses in 72% of immuno-suppressed patients [105]. A small retrospective study showed treatment with LAMB to be effective in reducing mortality [106]. LAMB is recommended in doses of at least 5 mg/kg [74] (B-III). The efficacy of posaconazole in a salvage therapy regimen was analyzed in two studies resulting in overall response rates (CR and PR) of 79 and 60%, respectively [107,108]. It is recommended by AGIHO by A-III level.

In patients with rhino–orbital–cerebral mucormycosis, combination polyene–caspofungin therapy resulted in superior success and prolonged overall survival combined with patients treated with polynemonotherapy [109]. However, further studies are needed to assess the definite role of combination therapy in this challenging infection.

Duration of therapy

As yet, the optimal duration of antifungal therapy has not been well defined. In any case, response assessment should be avoided before 14 consecutive days of antifungal treatment [74].
Clinicians should be cautious during neutrophil recovery, as radiological findings may apparently worsen with an increase of pulmonary lesions, which should not be misinterpreted as failure of antifungal treatment [101]. In general, antifungal treatment should be assured until complete resolution of lesions or reductions of residual scarring (B-III, AGIHO) [74].

Future perspective
Over the last decade, there have been made major advances in diagnostics of invasive fungal infections. Owing to improved diagnostic methods, IFI may be diagnosed earlier and, thus, antifungal treatment can be initiated more timely. Future research should address the development of newer more sensitive and more fail-safe methods and on further improvement of PCR techniques and diagnostic adjuncts such as β-D-glucan and galactomannan. Today, clinicians have the choice among a broad armamentarium of antifungal drugs. Combination therapy still remains a subsidiary option for a few cases. Evidence-driven management of IFIs is becoming increasingly individualized, integrating host factors and pharmacologic and epidemiologic considerations. However, the optimal approach to IFIs remains to be resolved by prospective clinical studies. There is still an ongoing requirement for randomized trials in order to finally bring tailored therapies to each patient and further improve the outcome.

Not least, further progress in optimizing antifungal prophylaxis should result in significantly lowering the frequency of this potential devastating infection.

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No writing assistance was utilized in the production of this manuscript.

Executive summary
- Invasive fungal infections remain a life-threatening complication for immunocompromised patients. Along with improved diagnostic tools and better supportive care, mortality rates linked to those infections have been reduced.
- Timely beginning of antifungal treatment is crucial and may be life-saving in this critical situation.
- In candidemia, the former standard fluconazole has gained several novel competitors. As data in neutropenic patients remain rare, several studies are lined up to prove their efficacy.
- In invasive aspergillosis, the former gold standard of targeted therapy, amphotericin B deoxycholate, has been replaced with lipid formulations, novel class echinocandins and new triazoles. Voriconazole is recommended as the drug of choice for treatment of invasive aspergillosis in all current guidelines whereas liposomal amphotericin B remains an alternative option. Combination of antifungals is not routinely recommended, but is an option in the salvage therapy setting.
- Mucormycosis remains a rare but mostly fatal complication in which, in addition to antifungal therapy, surgical intervention is frequently essential.

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- of interest
- of considerable interest
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» Evaluation of risk factors for infection and inverse outcome in hematologic patients.


» Important work on candidemia in cancer patients.


» Large prospective registry study.


» Current trends in epidemiology of IFI in the USA.


» Shows current changes in epidemiology of candidiasis in cancer patients.


» Shows limitations of galactomannan assay in diagnosis of IA.
Current treatment of IFIs in immunocompromised patients


Key work regarding classification of IFI.


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Review: Clinical Trial Outcomes

Auberger & Lass-Flörl


Current recommendation of the German Society of Hematology and Oncology.


Important study that led to the approval of voriconazole as first-line option in IA.


Important work on outcome and prognostic factors in patients with IA in HSCT.


Important study on posaconazole in refractory patients.


Important study regarding combination therapy in IA.


Current Infectious Diseases Society of America guidelines on treatment of IA.


Demonstrates the importance of timely initiation of treatment in mucomycosis.


