TABLE 241-3 TREATMENT OF ASPERGILLOSIS[a]

Indication	Primary Treatment	Evidence Level[b]	Precautions	Secondary Treatment	Comments
Invasive[c]	Voriconazole	AI	Drug interactions (especially with rifampin), renal failure (IV only)	AmB, caspofungin, posaconazole, micafungin	As primary therapy, voriconazole carries 20% more responses than AmB. Consider initial combination therapy with an echinocandin in non-neutropenic patients.
Prophylaxis	Posaconazole, itraconazole solution	AI	Diarrhea and vomiting with itraconazole, vincristine interaction	Micafungin, aerosolized AmB	Some centers monitor plasma levels of itraconazole and posaconazole.
Single aspergilloma	Surgery	BII	Multicavity disease: poor outcome of surgery, medical therapy preferable	Itraconazole, voriconazole, intracavity AmB	Single large cavities with an aspergilloma are best resected.
Chronic pulmonary[c]	Itraconazole, voriconazole	BII	Poor absorption of itraconazole capsules with proton pump inhibitors or H_2 blockers	Posaconazole, IV AmB, IV micafungin	Resistance may emerge during treatment, especially if plasma drug levels are subtherapeutic.
ABPA/SAFS	Itraconazole	AI	Some glucocorticoid interactions, including with inhaled formulations	Voriconazole, posaconazole	Long-term therapy is helpful in most cases. No evidence indicates whether therapy modifies progression to bronchiectasis/fibrosis.

[a]For information on duration of therapy, see text. [b]Evidence levels are those used in treatment guidelines (TJ Walsh et al: Treatment of aspergillosis: Clinical practice guidelines of the Infectious Diseases Society of America [IDSA]. Clin Infect Dis 46:327, 2008). [c]An infectious disease consultation is appropriate for these patients.

Note: The oral dose is usually 200 mg bid for voriconazole and itraconazole and 400 mg bid for posaconazole suspension. The IV dose of voriconazole for adults is 6 mg/kg twice at 12-h intervals (loading doses) followed by 4 mg/kg q12h; a larger dose is required for children and teenagers. Plasma monitoring is helpful in optimizing the dosage. Caspofungin is given as a single loading dose of 70 mg and then at 50 mg/d; some authorities use 70 mg/d for patients weighing >80 kg, and lower doses are required with hepatic dysfunction. Micafungin is given as 50 mg/d for prophylaxis and as at least 150 mg/d for treatment; this drug has not yet been approved by the U.S. Food and Drug Administration (FDA) for this indication. AmB deoxycholate is given at a daily dose of 1 mg/kg if tolerated. Several strategies are available for minimizing renal dysfunction. Lipid-associated AmB is given at 3 mg/kg (AmBisome) or 5 mg/kg (Abelcet). Different regimens are available for aerosolized AmB, but none is FDA approved. Other considerations that may alter dose selection or route include age; concomitant medications; renal, hepatic, or intestinal dysfunction; and drug tolerability.

Abbreviations: AmB, amphotericin B; ABPA, allergic bronchopulmonary aspergillosis; SAFS, severe asthma with fungal sensitization.

heart valve, sinuses, and proximal areas of the lung; brain abscess; keratitis; and endophthalmitis. In allergic fungal sinusitis, removal of abnormal mucus and polyps, with local and occasionally systemic glucocorticoid treatment, usually leads to resolution. Persistent or recurrent signs and symptoms may require more extensive surgery (ethmoidectomy) and possibly local antifungal therapy. Surgery is problematic in chronic pulmonary aspergillosis, usually resulting in serious complications. Bronchial artery embolization is preferred for problematic hemoptysis.

PROPHYLAXIS

In situations in which moderate or high risk is predicted (e.g., after induction therapy for acute myeloid leukemia), the need for antifungal prophylaxis for superficial and systemic candidiasis and for invasive aspergillosis is generally accepted. Fluconazole is commonly used in these situations but has no activity against *Aspergillus* species. Itraconazole capsules are ineffective, and itraconazole solution offers only modest efficacy. Posaconazole solution is more effective. Some data support the use of IV micafungin. No prophylactic regimen is completely successful.

OUTCOME

Invasive aspergillosis is curable if immune reconstitution occurs, whereas allergic and chronic forms are not. The mortality rate for invasive aspergillosis is ~50% if the infection is treated but is 100% if the diagnosis is missed. Infection with a voriconazole-resistant strain carries a mortality rate of 88%. Cerebral aspergillosis, *Aspergillus* endocarditis, and bilateral extensive invasive pulmonary aspergillosis have very poor outcomes, as does invasive infection in persons with late-stage AIDS or relapsed uncontrolled leukemia and in recipients of allogeneic hematopoietic stem cell transplants.

The mortality rate for chronic cavitary pulmonary aspergillosis is ~30% 6 months after presentation, falling to ~15% annually thereafter. After 12 months with no antifungal therapy, 70% of patients have deteriorated and 30% are stable (Fig. 241-2). Therapy fails in ~30% of recipients of antifungal therapy and still more often if azole resistance is present.

Both ABPA and SAFS patients respond to antifungal therapy; ~60% respond to itraconazole and ~80% to voriconazole and posaconazole (if tolerated). If the severity of asthma declines, the inhaled glucocorticoid dose can be reduced and oral glucocorticoids can be stopped.

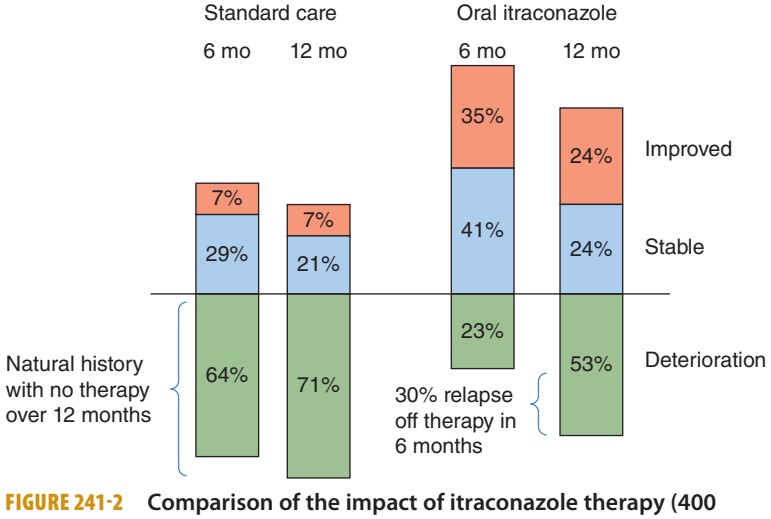

FIGURE 241-2 Comparison of the impact of itraconazole therapy (400 mg/d) and standard care on chronic cavitary pulmonary aspergillosis at 6 and 12 months. *(After R Agarwal et al: Itraconazole in chronic cavitary pulmonary aspergillosis: a randomised controlled trial and systematic review of literature. Mycoses 56:559, 2013.)*