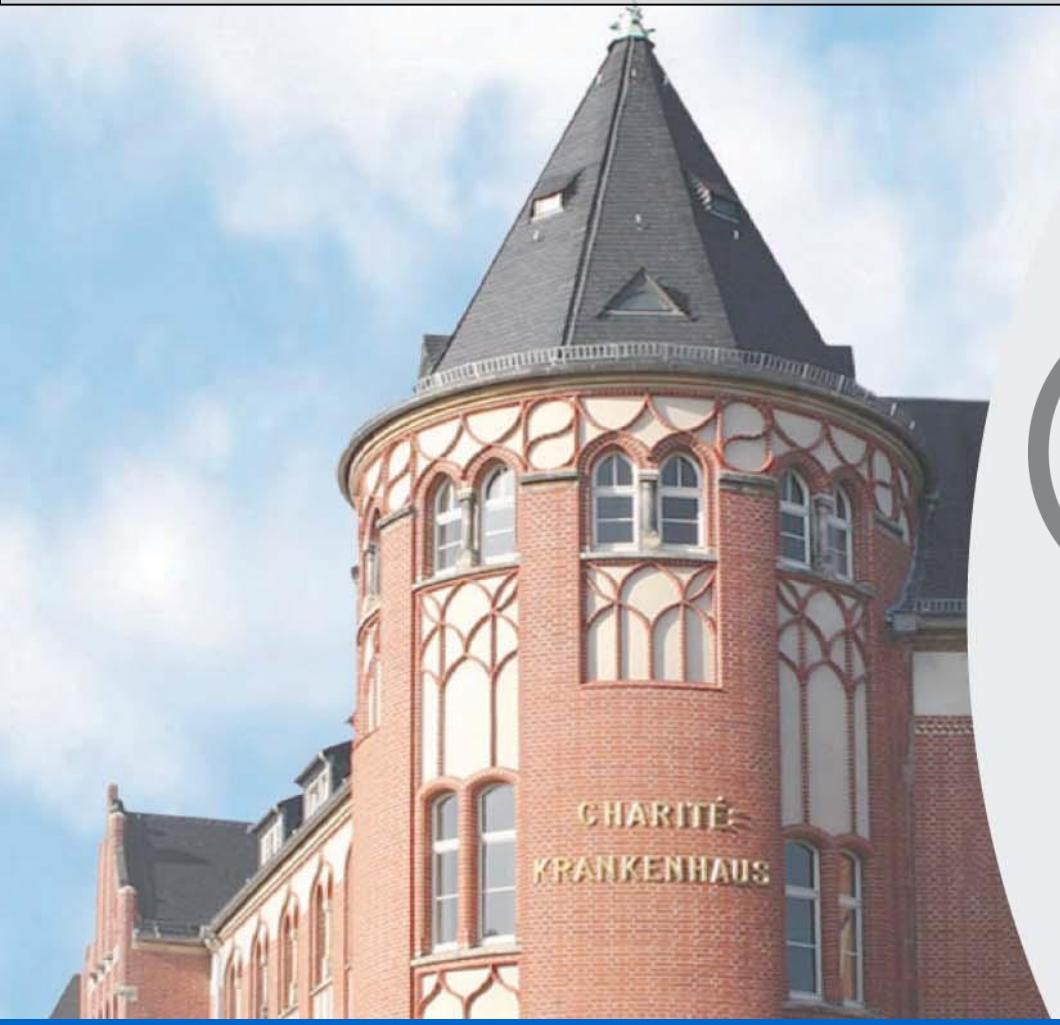
IDSA-Aspergillus Leitlinie



CHARITÉ
UNIVERSITÄTSMEDIZIN BERLIN

PD Dr. Stefan Schwartz
Medizinische Klinik m.S.
Hämatologie, Onkologie
Campus Benjamin Franklin

Treatment of Aspergillosis: Clinical Practice Guidelines of the Infectious Diseases Society of America

Thomas J. Walsh,[1,a] Elias J. Anaissie,[2] David W. Denning,[13] Raoul Herbrecht,[14] Dimitrios P. Kontoyiannis,[3] Kieren A. Marr,[5] Vicki A. Morrison,[6,7] Brahm H Segal,[8] William J. Steinbach,[9] David A. Stevens,[10,11] Jo-Anne van Burik,[7] John R. Wingard,[12] and Thomas F. Patterson[4,a]

34 Seiten

Walsh TJ, et al. *Clin Infect Dis* 2008; 46: 327-60

Practice Guidelines for the Diagnosis and Management of Aspergillosis: 2016 Update by the Infectious Diseases Society of America

Thomas F. Patterson,[1,a] George R. Thompson III,[2] David W. Denning,[3] Jay A. Fishman,[4] Susan Hadley,[5,b] Raoul Herbrecht,[6] Dimitrios P. Kontoyiannis,[7] Kieren A. Marr,[8] Vicki A. Morrison,[9] M. Hong Nguyen,[10] Brahm H. Segal,[11] William J. Steinbach,[12] David A. Stevens,[13] Thomas J. Walsh,[14] John R. Wingard,[15] Jo-Anne H. Young,[16] and John E. Bennett[17,a]

60 Seiten

Patterson TF, et al. *Clin Infect Dis* 2016; 63: e1-60

Graduierung Empfehlungen

2008 → **2016**

Table 1. Infectious Diseases Society of America–United States Public Health Service grading system for ranking recommendations in clinical guidelines.

Category, grade	Definition
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
Quality of evidence	
I	Evidence from ≥1 properly randomized, controlled trial
II	Evidence from ≥1 well-designed clinical trial, without randomization; from cohort or case-controlled analytic studies (preferably from >1 center); from multiple time-series; or from dramatic results from uncontrolled experiments
III	Evidence from opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees

- **strong**
- **weak**

- **high**
- **moderate**
- **low**
- **very low**

Walsh TJ, et al. *Clin Infect Dis* 2008; 46: 327-60
Kish MA *Clin Infect Dis* 2001 32: 851

US GRADE Network
www.gradeworkinggroup.org/

Empfehlungsgrade

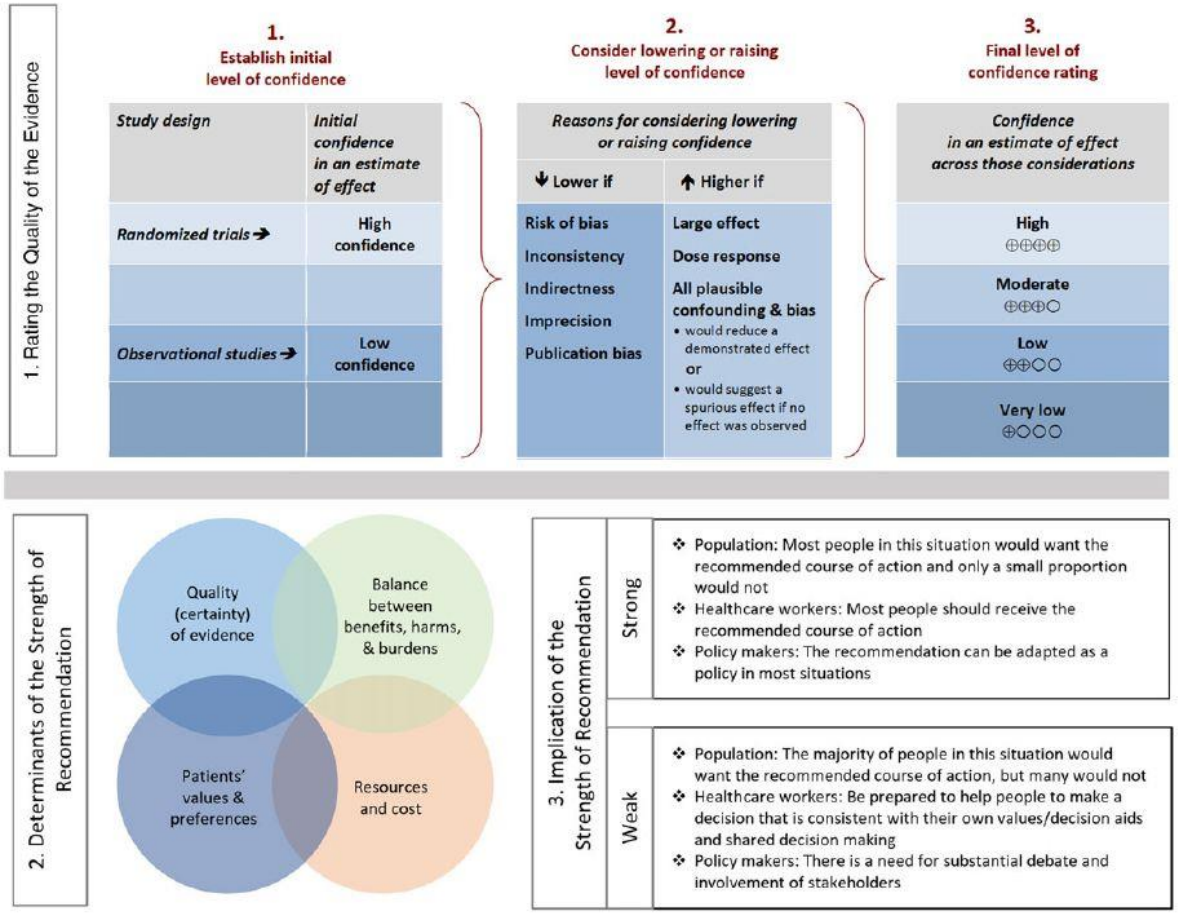


Figure 1. Approach and implications to rating the quality of evidence and strength of recommendations using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) methodology (unrestricted use of the figure granted by the US GRADE Network) [1].

US GRADE Network. Approach and implications to rating the quality of evidence and strength of recommendations using the GRADE methodology (www.gradeworkinggroup.org/).

Serologische Diagnostik

How Should Galactomannan and (1 → 3)-β-D-Glucan Be Used for the Diagnosis of Aspergillosis?

Recommendations.

9. Serum and BAL galactomannan (GM) is recommended as an accurate marker for the diagnosis of IA in adult and pediatric patients when used in certain patient subpopulations (hematologic malignancy, HSCT) *(strong recommendation; high-quality evidence).*
10. GM is not recommended for routine blood screening in patients receiving mold-active antifungal therapy or prophylaxis, but can be applied to bronchoscopy specimens from those patients *(strong recommendation; high-quality evidence).*
11. GM is not recommended for screening in SOT recipients or patients with chronic granulomatous disease (CGD) *(strong recommendation; high-quality evidence).*
12. Serum assays for (1 → 3)-β-D-glucan are recommended for diagnosing IA in high-risk patients (hematologic malignancy, allogeneic HSCT), but are not specific for *Aspergillus (strong recommendation; moderate-quality evidence).*

Molekulare Diagnostik

What Is the Diagnostic Value of Nucleic Acid Testing in Clinical Specimens?

Recommendations.

7. There was debate among the committee members regarding the clinical utility of blood-based polymerase chain reaction (PCR) in diagnosing IA, and experts were not in agreement.

8. As research in the area continues, we recommend that clinicians choosing to use PCR assays employ them carefully in the management of individual patients on a case-by-case basis. Clinicians should be aware of the methodologies and performance characteristics of the specific assay used, and interpret results accordingly. When PCR assays are used, results should be considered in conjunction with other diagnostic tests and the clinical context *(strong recommendation; moderate-quality evidence).*

Patterson TF, et al. *Clin Infect Dis* 2016; 63: e1-60

Radiologische Diagnostik

What Is the Approach to the Radiographic Diagnosis of Invasive Pulmonary Aspergillosis?

Recommendations.

13. We recommend performing a chest computed tomographic (CT) scan whenever there is a clinical suspicion for IPA regardless of chest radiograph results (*strong recommendation; high-quality evidence*).
14. Routine use of contrast during a chest CT scan for a suspicion of IPA is not recommended (*strong recommendation; moderate-quality evidence*). Contrast is recommended when a nodule or a mass is close to a large vessel (*strong recommendation; moderate-quality evidence*).
15. We suggest a follow-up chest CT scan to assess the response of IPA to treatment after a minimum of 2 weeks of treatment; earlier assessment is indicated if the patient clinically deteriorates (*weak recommendation; low-quality evidence*). When a nodule is close to a large vessel, more frequent monitoring may be required (*weak recommendation; low-quality evidence*).

Übersicht Therapie

Table 1. Summary of Recommendations for the Treatment of Aspergillosis

Condition	Therapy: Primary	Therapy: Alternative	Comments
Invasive syndromes of *Aspergillus*			
IPA	Voriconazole (6 mg/kg IV every 12 h for 1 d, followed by 4 mg/kg IV every 12 h; oral therapy can be used at 200–300 mg every 12 h or weight based dosing on a mg/kg basis); see text for pediatric dosing	Primary: Liposomal AmB (3–5 mg/kg/day IV), isavuconazole 200 mg every 8 h for 6 doses, then 200 mg daily Salvage: ABLC (5 mg/kg/day IV), caspofungin (70 mg/day IV × 1, then 50 mg/day IV thereafter), micafungin (100–150 mg/day IV), posaconazole (oral suspension: 200 mg TID; tablet: 300 mg BID on day 1, then 300 mg daily, IV: 300 mg BID on day 1, then 300 mg daily, itraconazole suspension (200 mg PO every 12 h)	Primary combination therapy is not routinely recommended; addition of another agent or switch to another drug class for salvage therapy may be considered in individual patients; dosage in pediatric patients for voriconazole and for caspofungin is different than that of adults; limited clinical experience is reported with anidulafungin; dosage of posaconazole in pediatric patients has not been defined
Invasive sinus aspergillosis	Similar to IPA	Similar to IPA	Surgical debridement as an adjunct to medical therapy
Tracheobronchial aspergillosis	Similar to IPA	Adjunctive inhaled AmB may be useful	Similar to IPA
Aspergillosis of the CNS	Similar to IPA	Similar to IPA Surgical resection may be beneficial in selected cases	This infection is associated with the highest mortality among all of the different patterns of IA; drug interactions with anticonvulsant therapy
Aspergillus infections of the heart (endocarditis, pericarditis, and myocarditis)	Similar to IPA	Similar to IPA	Endocardial lesions caused by *Aspergillus* species require surgical resection; *Aspergillus* pericarditis usually requires pericardiectomy
Aspergillus osteomyelitis and septic arthritis	Similar to IPA	Similar to IPA	Surgical resection of devitalized bone and cartilage is important for curative intent
Aspergillus infections of the eye (endophthalmitis and keratitis)	Systemic IV or oral voriconazole plus intravitreal AmB or voriconazole indicated with partial vitrectomy	Similar to invasive pulmonary aspergillosis; limited data with echinocandins and poor ocular penetration by this class	Systemic therapy may be beneficial in management of *Aspergillus* endophthalmitis; ophthalmologic intervention and management is recommended for all forms of ocular infection; topical therapy for keratitis is indicated
Cutaneous aspergillosis	Similar to IPA	Similar to IPA	Surgical resection is indicated where feasible
Aspergillus peritonitis	Similar to IPA	Similar to IPA	Removal of peritoneal dialysis catheter is essential
Empiric and preemptive antifungal therapy	For empiric antifungal therapy, Liposomal AmB (3 mg/kg/day IV), caspofungin (70 mg day 1 IV and 50 mg/day IV thereafter), micafungin (100 mg day), voriconazole (6 mg/kg IV every 12 h for 1 day, followed by 4 mg/kg IV every 12 h; oral therapy can be used at 200–300 mg every 12 h or 3–4 mg/kg q 12 h)		Preemptive therapy is a logical extension of empiric antifungal therapy in defining a high-risk population with evidence of invasive fungal infection (eg, pulmonary infiltrate or positive GM assay result)
Prophylaxis against IA	Posaconazole: Oral suspension: 200 mg TID Tablet: 300 mg BID on day 1, then 300 mg daily IV: 300 mg BID on day 1, then 300 mg daily	Voriconazole (200 mg PO BID), itraconazole suspension (200 mg PO every 12 h); micafungin (50–100 mg/day), caspofungin (50 mg/day)	Efficacy of posaconazole prophylaxis demonstrated in high-risk patients (patients with GVHD and neutropenic patients with AML or MDS)
Saprophytic or colonizing syndromes of *Aspergillus*			
Aspergilloma	No therapy or surgical resection	Itraconazole or voriconazole; similar to IPA	The role of medical therapy in the treatment of aspergilloma is uncertain; penetration into preexisting cavities may be minimal for AmB
Chronic cavitary pulmonary aspergillosis	Similar to IPA	Similar to IPA	Innate immune defects demonstrated in most of these patients; long-term therapy may be needed; surgical resection may lead to significant complications; anecdotal response to IFN-γ. Tranexamic acid may be helpful in management of hemoptysis
Allergic syndromes of *Aspergillosis*			
ABPA	Itraconazole	Oral voriconazole (200 mg PO every 12 h) or posaconazole (dosage depends on formulation)	Corticosteroids are a cornerstone of therapy for exacerbations; itraconazole has a demonstrable corticosteroid-sparing effect
Allergic rhinosinusitis caused by *Aspergillus*	Polypectomy and sinus washout with intranasal corticosteroids	Antifungal therapy reserved for refractory or relapsing cases	

Abbreviations: ABLC, amphotericin B lipid complex; ABPA, allergic bronchopulmonary aspergillosis; AmB, amphotericin B; AML, acute myelogenous leukemia; BID twice daily; CNS, central nervous system; GM, galactomannan; GVHD, graft-vs-host disease; IA, invasive aspergillosis; IFN-γ, interferon gamma; IPA, invasive pulmonary aspergillosis; IV, intravenous; MDS, myelodysplastic syndrome; PO, oral; TID, 3 times daily.

Antimykotische Therapie

Condition	Primary	Alternative
Invasive syndromes of *Aspergillus*		
IPA	Voriconazole (6 mg/kg IV every 12 h for 1 d, followed by 4 mg/kg IV every 12 h; oral therapy can be used at 200–300 mg every 12 h or weight based dosing on a mg/kg basis); see text for pediatric dosing	Primary: Liposomal AmB (3–5 mg/kg/day IV), isavuconazole 200 mg every 8 h for 6 doses, then 200 mg daily Salvage: ABLC (5 mg/kg/day IV), caspofungin (70 mg/day IV × 1, then 50 mg/day IV thereafter), micafungin (100–150 mg/day IV), posaconazole (oral suspension: 200 mg TID; tablet: 300 mg BID on day 1, then 300 mg daily, IV: 300 mg BID on day 1, then 300 mg daily, itraconazole suspension (200 mg PO every 12 h)
		Comments
Aspergillosis of the CNS	Similar to IPA Surgical resection may be beneficial in selected cases	Primary combination therapy is not routinely recommended; addition of another agent or switch to another drug class for salvage therapy may be considered in individual patients; dosage in pediatric patients for voriconazole and for caspofungin is different than that of adults; limited clinical experience is reported with anidulafungin; dosage of posaconazole in pediatric patients has not been defined
Empiric and preemptive antifungal therapy	For empiric antifungal therapy, Liposomal AmB (3 mg/kg/day IV), caspofungin (70 mg day 1 IV and 50 mg/day IV thereafter), micafungin (100 mg day), voriconazole (6 mg/kg IV every 12 h for 1 day, followed by 4 mg/kg IV every 12 h; oral therapy can be used at 200–300 mg every 12 h or 3–4 mg/kg q 12 h)	

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QT-Zeit unter Isavuconazol

IDSA 2016

pear modest. Interestingly, in contrast to other triazoles, isavuconazole could shorten the QTc interval; the clinical significance of this is unclear. There is no effect of the polymorphisms of

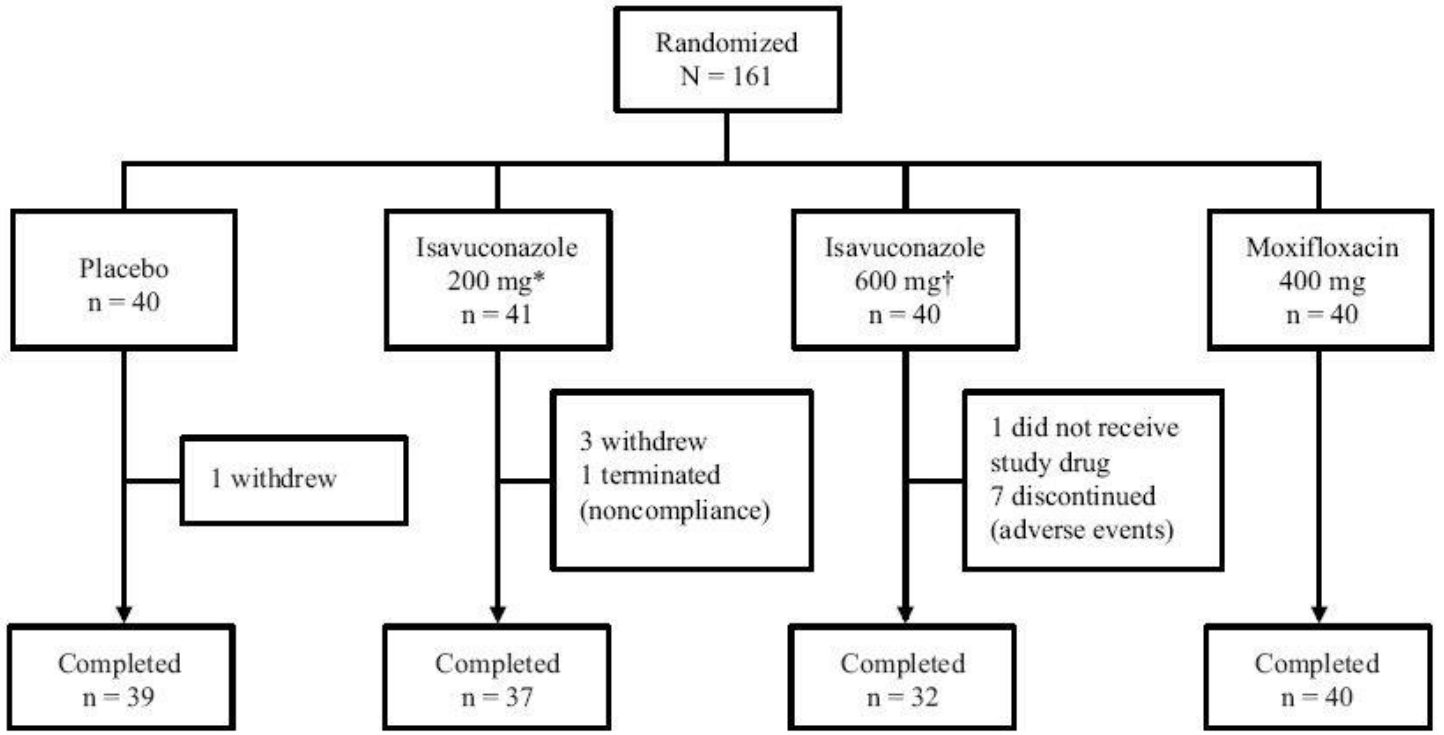


Figure 1 Subject disposition in the phase I clinical study. *Equivalent to the therapeutic dose of isavuconazonium sulfate 372 mg. †Equivalent to supra-therapeutic dose isavuconazonium sulfate 1,116 mg.

Keirns J, et al. *Clin Pharmacol Ther* 2017; Epub

QT-Zeit unter Isavuconazol

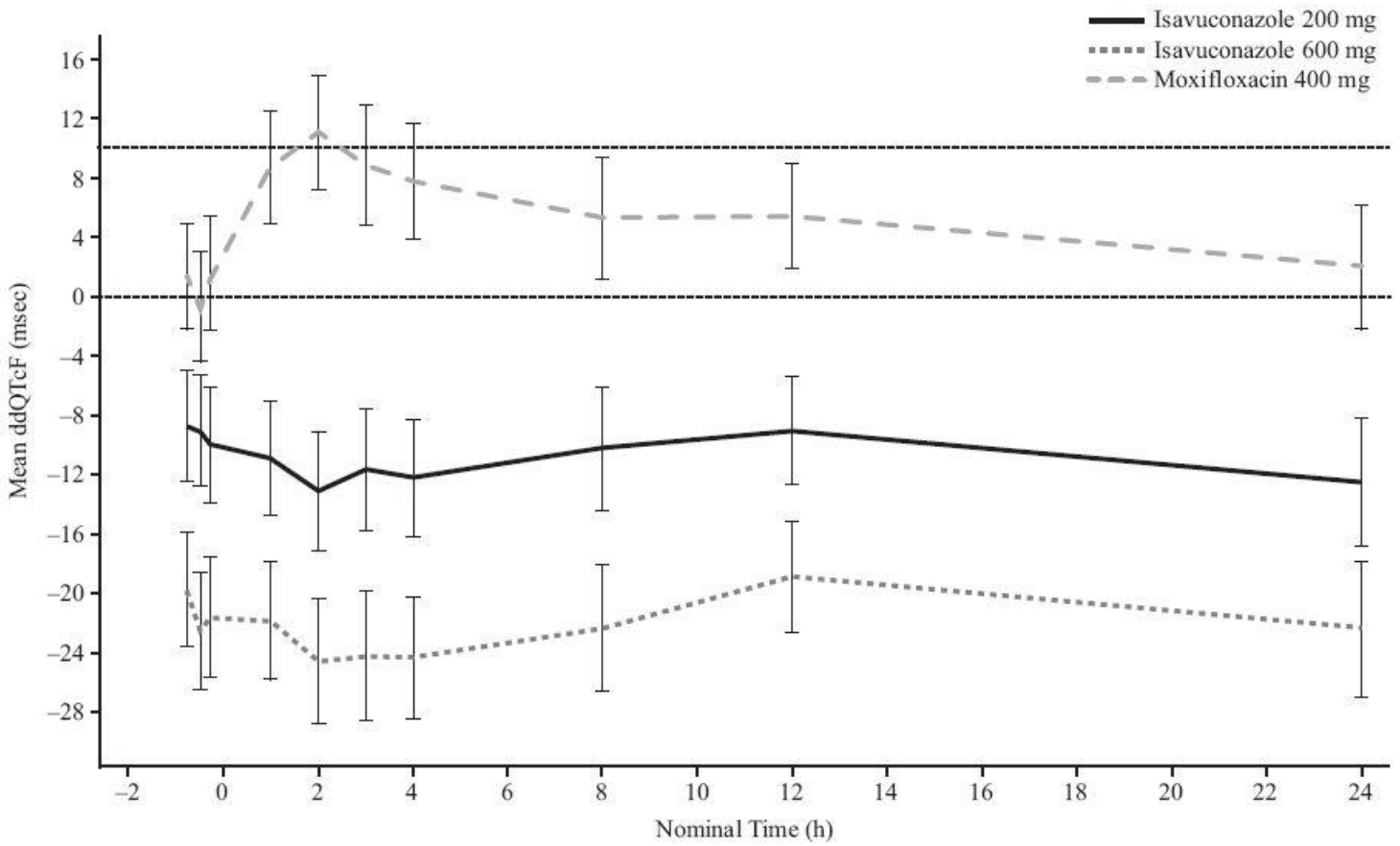


Figure 2 Mean change compared with placebo in baseline-adjusted* QTcF over time on Day 13 in the phase I clinical study. Error bars represent 90% CI. *QTcF*, Fridericia-corrected QT interval; *ddQTcF*, time-matched, drug–placebo difference in QTcF interval, baseline-adjusted. Zero on x-axis represents time of Day 13 dose; horizontal dotted line represents threshold for significant prolongation of QTcF interval. *Baseline was defined as time-matched measurement on Day −1.

Keirns J, et al. *Clin Pharmacol Ther* 2017; Epub

Chirurgie - IDSA 2008

Lesions contiguous with the great vessels or pericardium, hemoptysis from a single cavitary lesion, or invasion of the chest wall (B-II)

Resection of a single pulmonary lesion prior to intensive chemotherapy or HSCT (B-II)

Table 3. Relative indications for surgery in treatment of invasive aspergillosis.

Condition	Surgical procedure	Comment
Pulmonary lesion in proximity to great vessels or pericardium	Resection of pulmonary lesion	May prevent erosion of pulmonary lesions into great vessels and into pericardial space
Pericardial infection	Pericardiectomy	Pericardiectomy reduces organism burden around heart and prevents tamponade
Invasion of chest wall from contiguous pulmonary lesion	Resection of pulmonary lesion	Resection of lesion may relieve pain and prevent pleurocutaneous fistula
Aspergillus empyema	Placement of chest tube	Reduces burden of organism in closed space
Persistent hemoptysis from a single cavitary lesion	Resection of cavity	May prevent exsanguinating hemoptysis; other measures to reduce hemoptysis include embolization of involved blood vessel and cauterization; however, recurrence of bleeding is possible
Infection of skin and soft tissues	Debridement, wide margin surgical resection	Surgical judgment used in extent of debridement and resection, if indicated
Infected vascular catheters and prosthetic devices	Removal of catheters and devices	Removal of infected catheters and devices provides definitive eradication
Endocarditis	Resection of vegetation and infected valve	Vegetations may be valvular or mural; single mural lesions are resectable, particularly if pedunculated
Osteomyelitis	Debridement of infected bone	Debridement of necrotic and infected bone reduces organism burden and allows better drug penetration; surgical judgment determines extent of debridement
Sinusitis	Resection of infected tissues	Extent of debridement may vary from no intervention to wide resection, depending on surgical judgment
Cerebral lesions	Resection of infected tissue	Extent of debridement may vary from no intervention to complete resection, depending on location, neurological sequelae, accessibility, and surgical judgment

NOTE. Indications depend on multiple variables, severity of lesion, surgical judgment, and the ability of the patient to tolerate the operative procedure, as well as the potential role of alternative medical therapy.

Chirurgie – IDSA 2016

36. Surgery for aspergillosis should be considered for localized disease that is easily accessible to debridement (eg, invasive fungal sinusitis or localized cutaneous disease) *(strong recommendation; low-quality evidence)*. The benefit for IA in other settings such as in the treatment of endocarditis, osteomyelitis, or focal central nervous system (CNS) disease appears rational. Other indications are less clear and require consideration of the patient's immune status, comorbidities, confirmation of a single focus, and the risks of surgery.

Surgical intervention is frequently discussed during the care of patients with CNS aspergillosis as resection of infected tissue or abscesses eliminates areas containing viable fungi. A mortality benefit of surgery for the management of cerebral lesions, in combination with antifungal therapy with voriconazole, has been shown in a retrospective study of 81 patients [432]. Although this study was subject to selection bias for those patients who were ultimately able to undergo surgical intervention, a benefit of voriconazole followed by surgical intervention was suggested (HR, 2.1; 95% CI, 1.1–3.9; $P = .2$). Surgical intervention is also a useful adjunct in the management of CNS aspergillosis with contiguous infections of the paranasal sinuses or vertebral bodies and should be pursued in these circumstances when feasible.

What Is the Role of Surgery in Aspergillosis of the Paranasal Sinuses?

Recommendation.

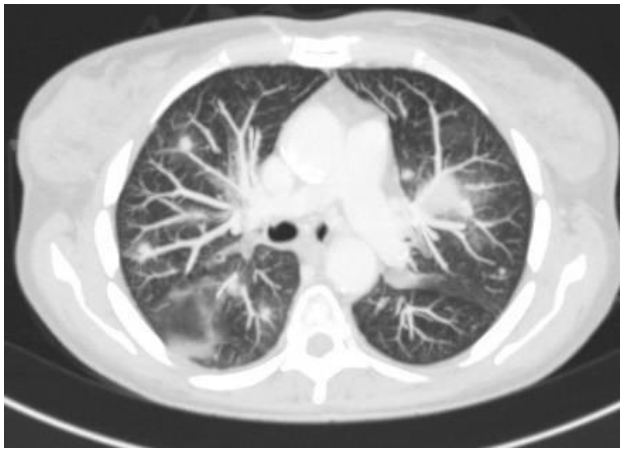
52. We recommend that both surgery and either systemic voriconazole or a lipid formulation of AmB formulation be used in invasive *Aspergillus* fungal sinusitis but that surgical removal alone can be used to treat *Aspergillus* fungal ball of the paranasal sinus. Enlargement of the sinus ostomy may be needed to improve drainage and prevent recurrence *(strong recommendation; moderate-quality evidence)*.

Surgery: In general, surgical treatment of aspergillosis should be considered for localized disease that is accessible to debridement. Emergent debridement of sinus aspergillosis can be life-saving and limit extension to the orbit and brain. Localized cutaneous aspergillosis should also be debrided. CNS aspergillosis is a devastating complication; neurosurgical removal combined with antifungal therapy may be life-saving, although the expected postsurgical neurologic outcome should also be considered during the decision process. Surgical resection of pulmonary lesions due to *Aspergillus* species can provide a definitive diagnosis and can potentially completely eradicate a localized infection. Surgical therapy may be useful in patients with lesions that are contiguous with the great vessels or the pericardium, uncontrolled bleeding, or invasion of the pleural space and chest wall. Intervention should also be considered for localized pulmonary aspergillosis refractory to antifungal therapy [387].

Another consideration for surgery is the resection of a single pulmonary lesion prior to intensive chemotherapy or HSCT. However, the favorable experience of HSCT in patients with prior IA suggests that antifungal therapy alone may be effective [367, 388–391]. An acceptable approach in patients with pretransplant aspergillosis is close CT monitoring without surgical resection in the absence of additional complications, such as uncontrolled bleeding or chest wall extension. Decisions concerning surgical therapy should be individualized to account for a number of variables, including the degree of resection (eg, wedge resection vs pneumonectomy), potential impact of delays in chemotherapy, comorbidities, performance status, the goal of antineoplastic therapy (eg, curative vs palliative), and unilateral vs bilateral lesions.

Pat. mit AML + Lungeninfiltrat

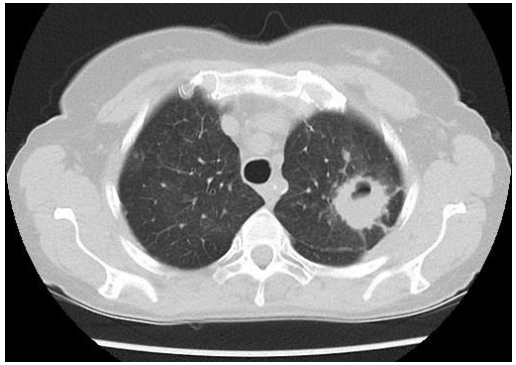
♀ 60 y, AML, HiDAC Konsolidierung

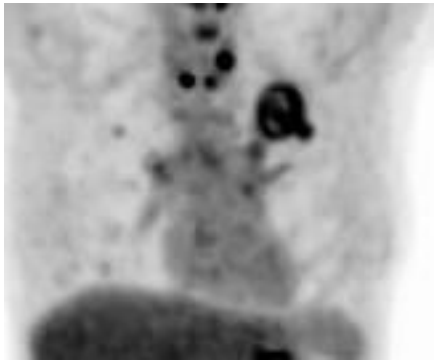


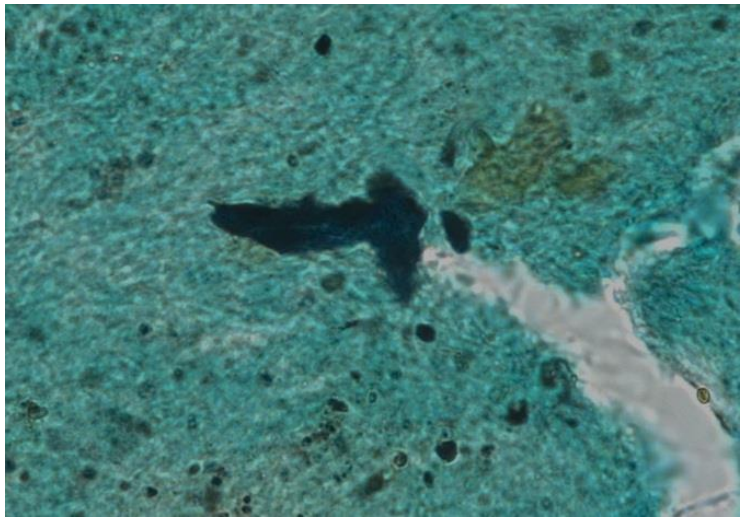
Serum Asp-GM –
keine Bronchoskopie

Resektion OL links
PCR + für *Rhizopus sp.*

Voriconazol >5 Monate







Kombinationstherapie

28. Combination antifungal therapy with voriconazole and an echinocandin may be considered in select patients with documented IPA (*weak recommendation; moderate-quality evidence*).

icity differences. This study adds to prior preclinical and observational clinical studies that suggest potential benefits for combination therapy with voriconazole and an echinocandin [198, 356, 363]. For this reason, the committee suggests consideration for an echinocandin with voriconazole for primary therapy in the setting of severe disease, especially in patients with hematologic malignancy and those with profound and persistent neutropenia.

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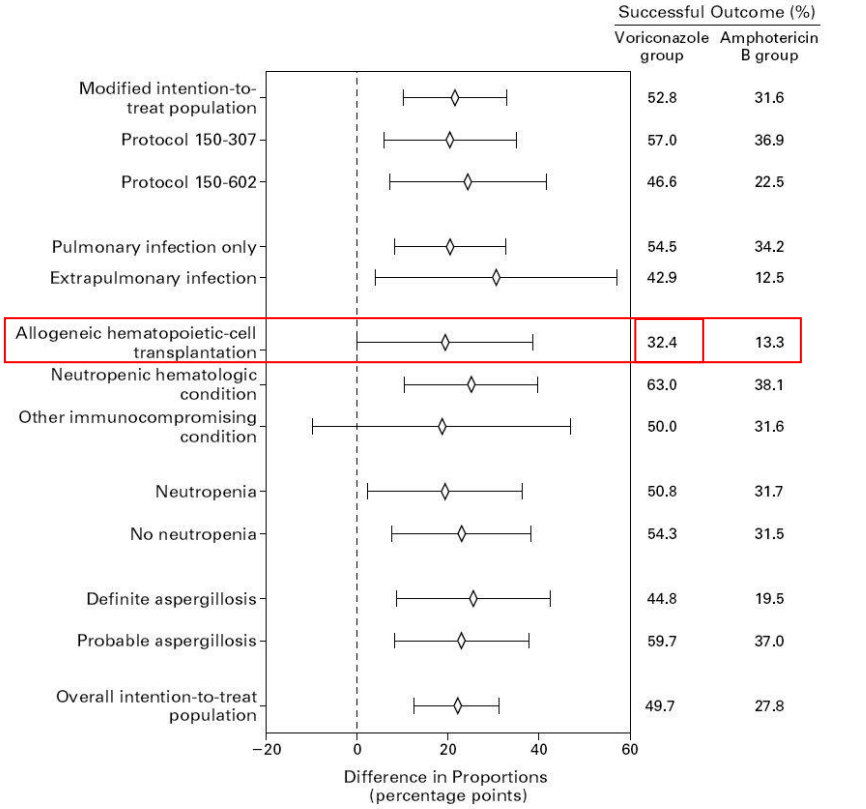


Figure 1. Response Rates in the Modified Intention-to-Treat Population, According to the Study Protocol, Site of Infection, Underlying Condition, Neutropenic Status, and Degree of Certainty of the Diagnosis, and in the Intention-to-Treat Population.

Results are expressed as the differences (with 95 percent confidence intervals) between the voriconazole group and the amphotericin B group in the rate of successful outcomes.

Herbrecht R, et al. *N Engl J Med.* 2002;347:408-415.

Therapie nach Azolprophylaxe

MANAGEMENT OF BREAKTHROUGH INFECTION

How Should Breakthrough Aspergillosis Be Managed?
Recommendation.

73. We suggest an individualized approach that takes into consideration the rapidity and severity of infection and local epidemiology. As principles, we recommend an aggressive and prompt attempt to establish a specific diagnosis with bronchoscopy and/or CT-guided biopsy for peripheral lung lesions. Documentation of serum azole levels should be verified if TDM is available for patients receiving mold-active triazoles. Antifungal therapy should be empirically changed to an alternative class of antifungal with *Aspergillus* activity. Other considerations include reduction of underlying immunosuppression if feasible, and susceptibility testing of any *Aspergillus* isolates recovered from the patient *(weak recommendation; moderate-quality evidence)*.

Weitere Unsicherheiten …

When Is It Safe to Proceed With Chemotherapy or Transplantation in a Patient With Invasive Aspergillosis?

Recommendations.

37. IA is not an absolute contraindication to additional chemotherapy or HSCT *(strong recommendation; moderate-quality evidence).*
38. Decisions about when to proceed with additional chemotherapy or HSCT following the diagnosis of aspergillosis should involve both infectious diseases specialists and hematologists/oncologists. These decisions must consider the risk of progressive aspergillosis during periods of subsequent antineoplastic treatment vs the risk of death from the underlying malignancy if this treatment is delayed *(strong recommendation; low-quality evidence).*

Pädiatrische Patienten

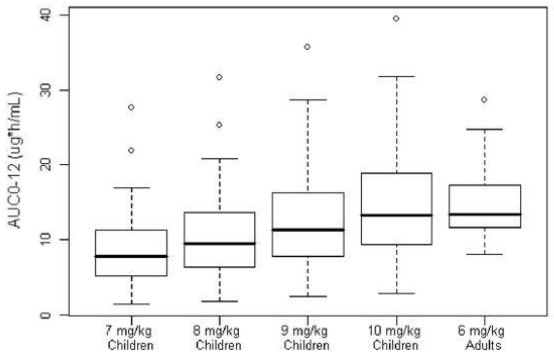
45. Treatment of aspergillosis in children uses the same recommended therapies as in adult patients; however, the dosing is different and for some antifungals is unknown *(strong recommendation; high-quality evidence)*.

Integrated Population Pharmacokinetic Analysis of Voriconazole in Children, Adolescents, and Adults

Lena E. Friberg,[a] Patanjali Ravva,[b] Mats O. Karlsson,[a] and Ping Liu[c]

Department of Pharmaceutical Biosciences, Uppsala University, Uppsala, Sweden[a]; Pharmacometrics, Primary Care, Pfizer Inc., Groton, Connecticut, USA[b]; and Clinical Pharmacology, Specialty Care, Pfizer Inc., Groton, Connecticut, USA[c]

a) Day 1 IV



b) Day 7 IV (Steady State)

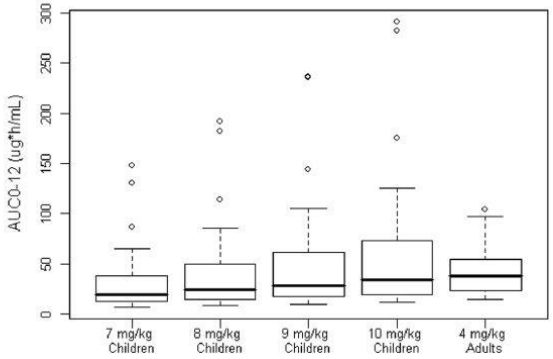


TABLE 5 Voriconazole doses in children and adolescents providing exposures comparable to those in adults

	Matching dose (q12h)			
		Maintenance dose		
Group	Loading dose (i.v.)	i.v.	i.v.	Oral
Children (2 to <12 yr old) and young adolescents (12 to 14 yr old weighing <50 kg)	9 mg/kg	8 mg/kg	4 mg/kg	9 mg/kg (maximum dose of 350 mg)
Other adolescents (12–14 yr old weighing ≥50 kg and 15–16 years old) and adults	6 mg/kg	4 mg/kg	3 mg/kg	200 mg

Friberg LE, et al. *Antimicrob Agents Chemother Dis* 2012; 56: 3032-42

Therapiedauer

IDSA 2008

[a] Duration of therapy for most conditions for aspergillosis has not been optimally defined. Most experts attempt to treat pulmonary infection until resolution or stabilization of all clinical and radiographic manifestations. Other factors include site of infection (e.g., osteomyelitis), level of immunosuppression, and extent of disease. Reversal of immunosuppression, if feasible, is important for a favorable outcome for invasive aspergillosis.

Duration of antifungal therapy for invasive pulmonary aspergillosis is not well defined. We generally recommend that treatment of invasive pulmonary aspergillosis be continued for a minimum of 6–12 weeks; in immunosuppressed patients, therapy should be continued throughout the period of immunosuppression and until lesions have resolved. Long-term therapy of invasive aspergillosis is facilitated by the availability of oral voriconazole in stable patients. **For patients with suc-**

IDSA 2016

Duration of antifungal therapy for IPA is not well defined. We generally recommend that treatment of IPA be continued for a minimum of 6–12 weeks, depending on the severity and continuation of immunosuppression, as well as the extent of resolution of clinical disease. Therapeutic monitoring of IPA in-

30. We recommend that treatment of IPA be continued for a minimum of 6–12 weeks, largely dependent on the degree and duration of immunosuppression, site of disease, and evidence of disease improvement (*strong recommendation; low-quality evidence*).

repair [426]. Duration of therapy for TBA is not well studied, but we recommend at least 3 months of systemic antifungal therapy with or without aerosolized AmB or until TBA is completely resolved, whichever is longer.

49. In lung transplant recipients, we recommend treatment with a systemic antimold antifungal for TBA, including saprophytic forms. We also recommend adjunctive inhaled AmB in the setting of TBA associated with anastomotic endobronchial ischemia or ischemic reperfusion injury due to airway ischemia associated with lung transplant *(strong recommendation; moderate-quality evidence).* Duration of antifungal therapy is at least 3 months or until TBA is completely resolved, whichever is longer.

Chronische/nicht-invasive Aspergillose

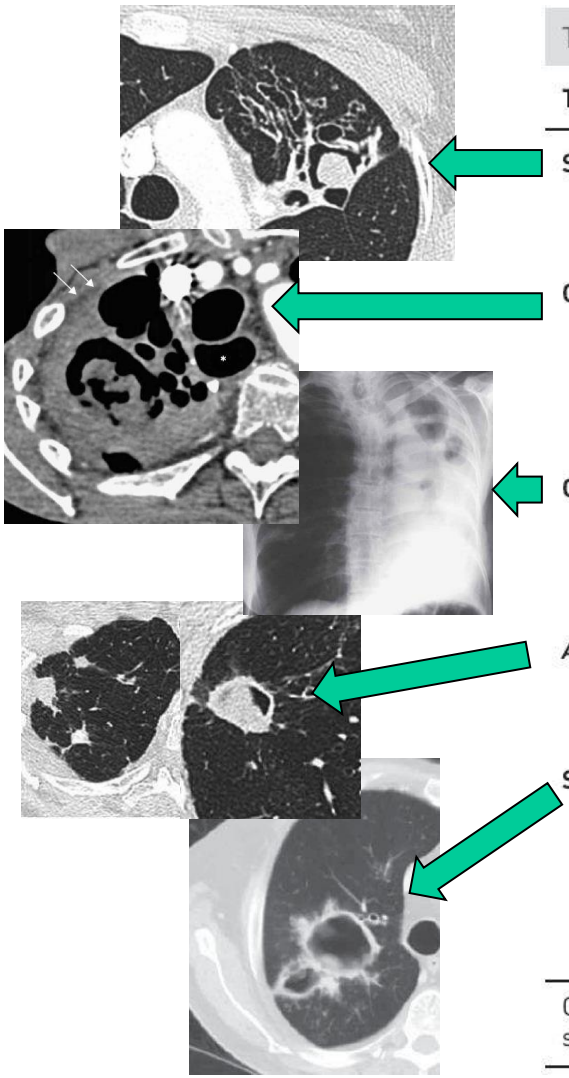
IDSA
No or little immunosuppression, underlying lung disease frequent

CPA = chronic pulmonary aspergillosis
- CCPA = chronic cavitary pulmonary aspergillosis
  -> CFPA = chronic fibrosing pulmonary aspergillosis
- single aspergilloma
- *Aspergillus* nodule

ABPA = allergic bronchopulmonary aspergillosis
AFRS = allergic fungal rhinosinusitis

Patterson TF, et al. *Clin Infect Dis* 2016; 63: e1-60

Chronisch/nicht-invasive Aspergillose



ESCMID/ERS Guideline

TABLE 3 Diagnostic criteria for different management of chronic pulmonary aspergillosis (CPA)

Term	Definition
Simple aspergilloma	Single pulmonary cavity containing a fungal ball, with serological or microbiological evidence implicating *Aspergillus* spp. in a non-immunocompromised patient with minor or no symptoms and no radiological progression over at least 3 months of observation.
CCPA	One or more pulmonary cavities (with either a thin or thick wall) possibly containing one or more aspergillomas or irregular intraluminal material, with serological or microbiological evidence implicating *Aspergillus* spp. with significant pulmonary and/or systemic symptoms and overt radiological progression (new cavities, increasing pericavitary infiltrates or increasing fibrosis) over at least 3 months of observation.
CFPA	Severe fibrotic destruction of at least two lobes of lung complicating CCPA leading to a major loss of lung function. Severe fibrotic destruction of one lobe with a cavity is simply referred to as CCPA affecting that lobe. Usually the fibrosis is manifest as consolidation, but large cavities with surrounding fibrosis may be seen.
***Aspergillus* nodule**	One or more nodules which may or may not cavitate are an unusual form of CPA. They may mimic tuberculoma, carcinoma of the lung, coccidioidomycosis and other diagnoses and can only be definitively diagnosed on histology. Tissue invasion is not demonstrated, although necrosis is frequent.
SAIA	Invasive aspergillosis, usually in mildly immunocompromised patients, occurring over 1–3 months, with variable radiological features including cavitation, nodules, progressive consolidation with "abscess formation". Biopsy shows hyphae in invading lung tissue and microbiological investigations reflect those in invasive aspergillosis, notably positive *Aspergillus* galactomannan antigen in blood (or respiratory fluids).

CCPA: chronic cavitary pulmonary aspergillosis; CFPA: chronic fibrosing pulmonary aspergillosis; SAIA: subacute invasive aspergillosis/chronic necrotising/semi-invasive.

Denning DW, et al. *Eur Respir J* 2016; 47: 45-68

Vielen Dank für die Aufmerk-samkeit!