Treatment Guidelines for Invasive Aspergillosis

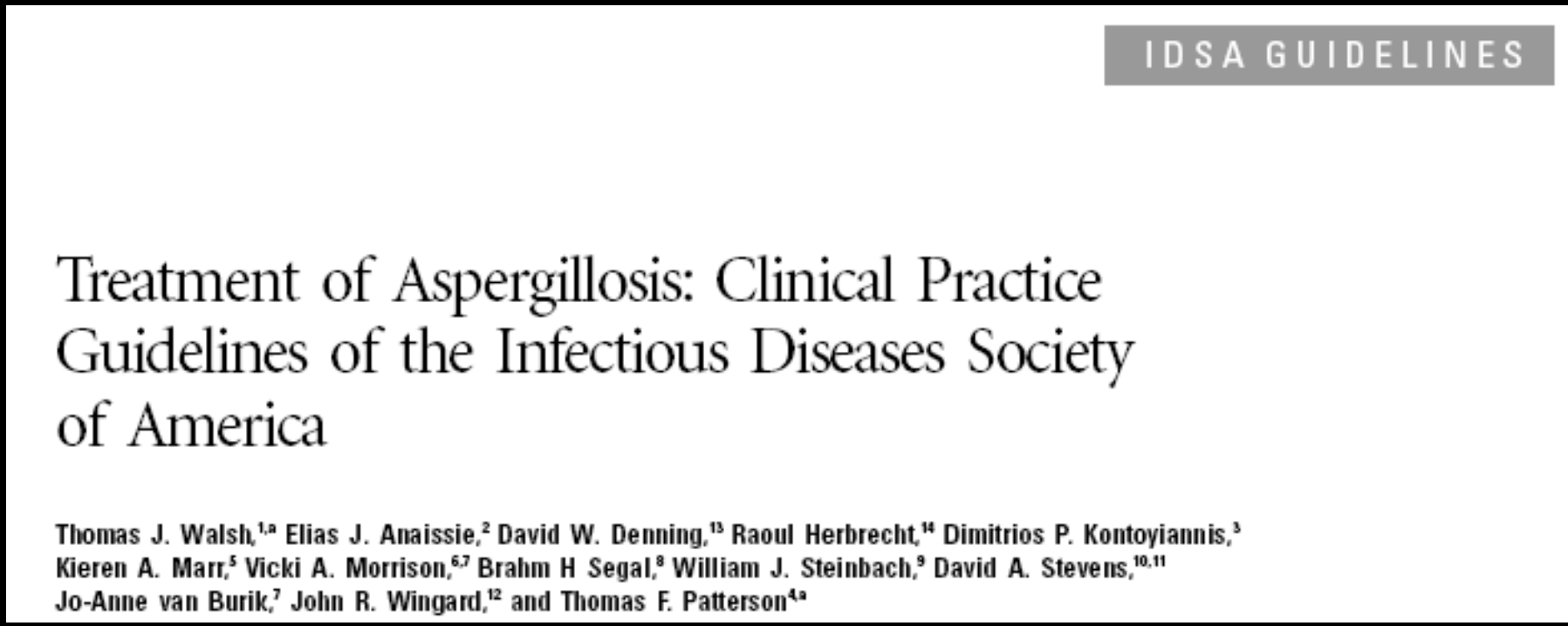
Thomas F. Patterson, MD
Professor of Medicine
Director, San Antonio Center for Medical Mycology

WE MAKE LIVES BETTER
UT HEALTH SCIENCE CENTER™
SAN ANTONIO

The University of Texas Health Science Center at San Antonio

S • A • C • M • M
San Antonio Center for Medical Mycology

IDSA Clinical Practice Guidelines for Aspergillosis 2008



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

S ◆ A ◆ C ◆ M ◆ M
San Antonio Center for Medical Mycology

Guidelines for Treatment of Invasive Aspergillosis

- Key recommendations:
  - How can we make an early diagnosis?
    - Role of radiology
    - Non-culture based methods
  - What are options for therapy?
    - Primary therapy
    - Salvage options
    - Combination therapy
  - Therapy for extrapulmonary infection
  - Management of chronic, saprophytic, & allergic conditions

S ◆ A ◆ C ◆ M ◆ M
San Antonio Center for Medical Mycology

Key recommendations: Diagnosis of Invasive Aspergillosis

- Importance of culture confirmation when possible
- Utility of "halo" sign in neutropenic patients
  - Not specific for *Aspergillus*
- Non-culture based methods to facilitate diagnosis
  - Galactomannan, (1→3)-β-D-glucan
  - PCR not yet established
- Possible impact of antifungal resistance

S ◆ A ◆ C ◆ M ◆ M
San Antonio Center for Medical Mycology

Screening for Invasive Aspergillosis using *Aspergillus* Platelia EIA

- Maertens et al (2001)
  - Sensitivity: 89%; Specificity: 98%
    - Serial testing needed for optimal results
- Herbrecht et al (2002); Marr et al (2004)
  - Limited sensitivity (43-70%); Better specificity (70-93%)
  - Lower cut-off on empirical antifungals or prophylaxis
    - Original criteria: Pos (Index 1.0-1.5) on 2 consecutive samples
    - US: Pos (0.5) on repeat testing (same sample)
    - EU: Pos (0.5-0.7); dynamic endpoint (Maertens, 2005)
- False-positive results (Verweij, 1998)
  - Weakly positive samples
  - Laboratory contamination
  - Cross-reactivity
  - Dietary
  - Piperacillin/Tazobactam (Viscoli, 2003; Sulahian, 2003)
  - Plasmalyte (Wheat, 2006)

Maertens J, et al. *Clin Infect Dis* 2005;41:1242-50; Marr KA, et al. *J Infect Dis* 2004;190:641-9; Herbrecht R, et al. *J Clin Oncol* 2002;20:1898-1906; Viscoli C, et al. *Clin Infect Dis* 2004;38:913-6

Utility of β-Glucan Detection in Invasive Fungal Infection

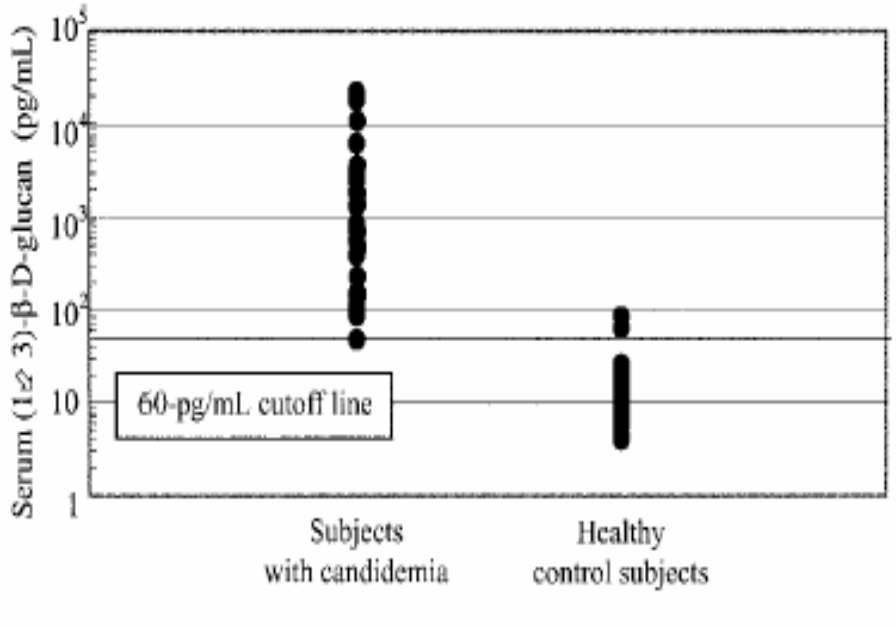


Figure 1. Serum glucan levels in 30 subjects with candidemia and 30 healthy control subjects.

- 30 candidemic pts/30 controls
  - Cut-off >60 pg/ml
- 283 pts AML/MDS (twice weekly samples)
  - Sensitivity: 20/20 IFI pts at least one positive
  - Specificity: 90%
  - Organisms detected: *Candida, Aspergillus, Trichosporon, Fusarium*
- 163 pt IFI/170 controls (single samples)
  - Sensitivity: 70%
  - Specificity: 87%

Note: IFI=invasive fungal infection

Obadasi Z et al. *Clin Infect Dis* 2004;39:199-205;
Ostrosky-Zeichner L et al. *Clin Infect Dis* 2005;41:654-9

S • A • C • M • M
San Antonio Center for Medical Mycology

PCR for Invasive Aspergillosis

Design	Sens (%)	Spec (%	Ref
Pan-fungal	100		;35:1353-60
Pan-fungal			001;113:180-4
Asp. sp.			713-9
Asp. sp.			3:428-35
Asp. sp.			
Asp. sp.			04;125:196-202
Asp. sp.	92	9	CID 20 :42:479-82

PCR not (*yet*) accepted for mycological criteria

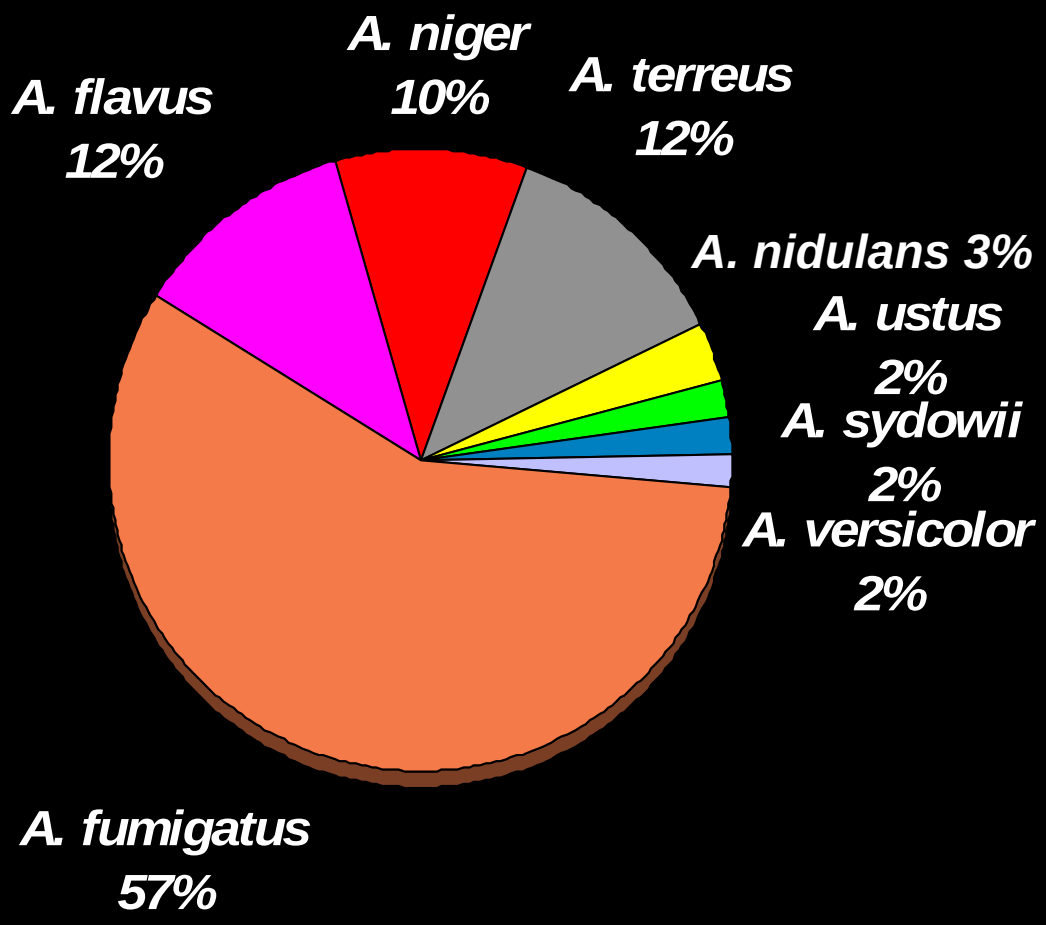
- Variable sensitivity / speci ity
- Limited per test positivity
- Technical false positives/negatives
- Lack of standardized targets/reagents
- Not externally validated

Donnelly JP. *Clin Infect Dis* 2006;42:487-9

S ◆ A ◆ C ◆ M ◆ M
San Antonio Center for Medical Mycology

Aspergillus spp. Isolates Submitted to San Antonio Fungus Testing Laboratory

918 Isolates; Jan. 2001-July 2004



AmB MLC >16

- *A. fumigatus* 24%

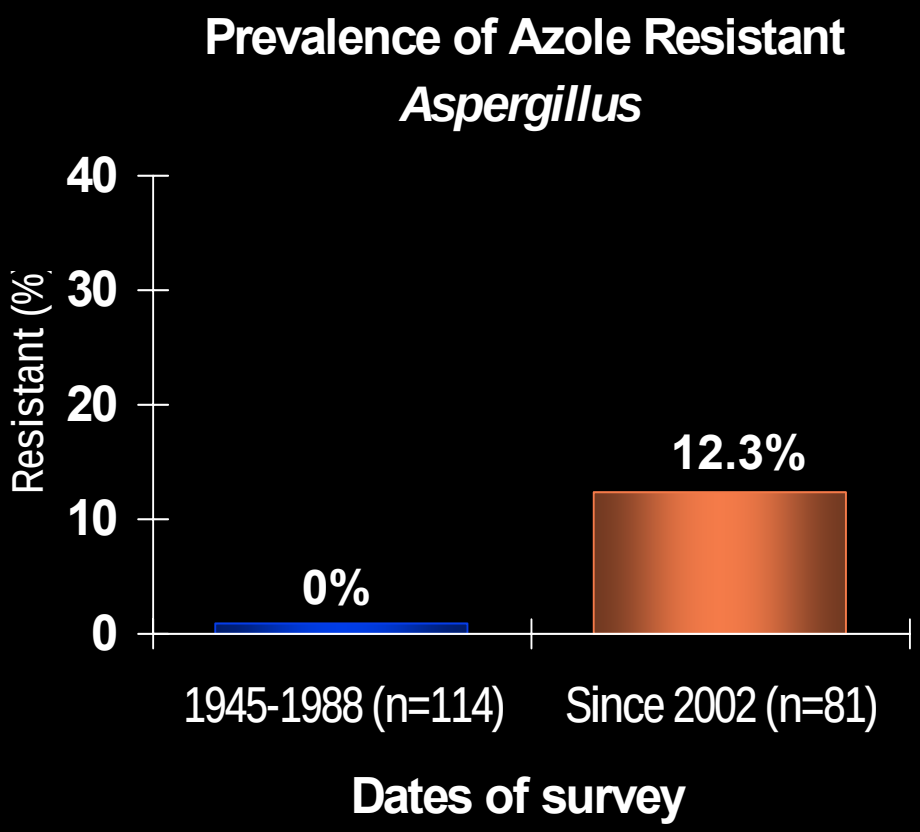
AmB MIC≥2

- *A. terreus* 90%
- *A. flavus* 51%
- *A. ustus* 50%

Sutton D et al, Advances Against *Aspergillus* 2004 (Abstract 16)

S ◆ A ◆ C ◆ M ◆ M
San Antonio Center for Medical Mycology

Azole Resistance in *Aspergillus*



- Detection of multi-azole resistant *Aspergillus* in Dutch medical centers since 2002:
  - Cross resistance to voriconazole, itraconazole, posaconazole, ravuconazole
  - MICs 0.5-16 µg/ml
- A new *cyp51A* gene mutation in 12 of 13 isolates; not clonal
- Associated with itraconazole prophylaxis in 4
- Responses in most patients with voriconazole or posaconazole

Verweij PE, et al. *NEJM* 2007;356:1481-3.

S ◆ A ◆ C ◆ M ◆ M
San Antonio Center for Medical Mycology

Key Recommendation: Primary Therapy of Invasive Aspergillosis

- Preferred therapy:

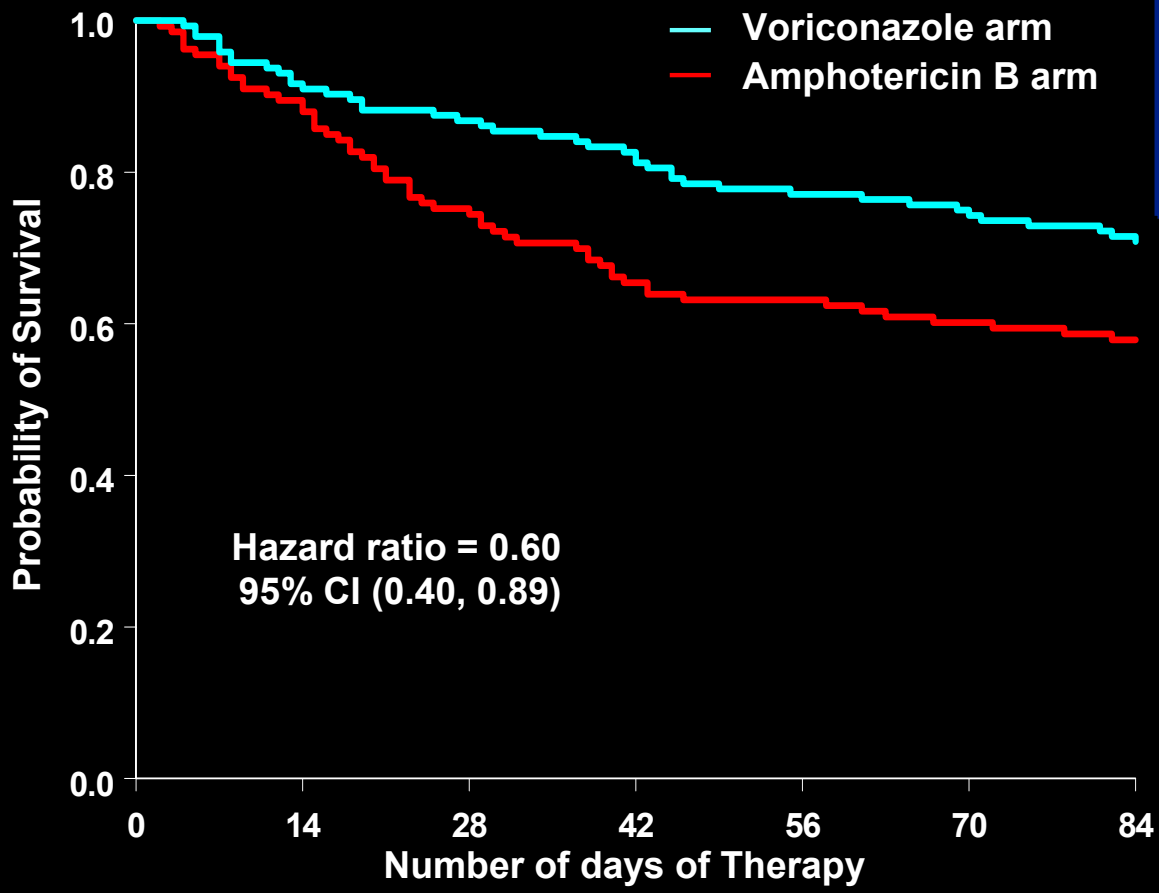
Voriconazole is recommended for the primary treatment of invasive aspergillosis in most patients (AI).

Key Recommendation: Primary Treatment of Invasive Aspergillosis

- Alternative Agents:

  A randomized trial comparing two dosages of liposomal amphotericin B showed similar efficacy in both arms, suggesting that liposomal therapy could be considered as alternative primary therapy in some patients (AI).

Global Comparative Aspergillosis Study: Survival Benefit of Voriconazole



Outcome at week 12	Vori Arm	AmB Arm
Survival	70.8%	57.9%
Response	56.8%	31.%

- ✓ Poor efficacy of AmB prior "gold standard"
- ✓ Vori recommended for primary therapy
- Importance of early therapy
- Limited success of rescue therapy

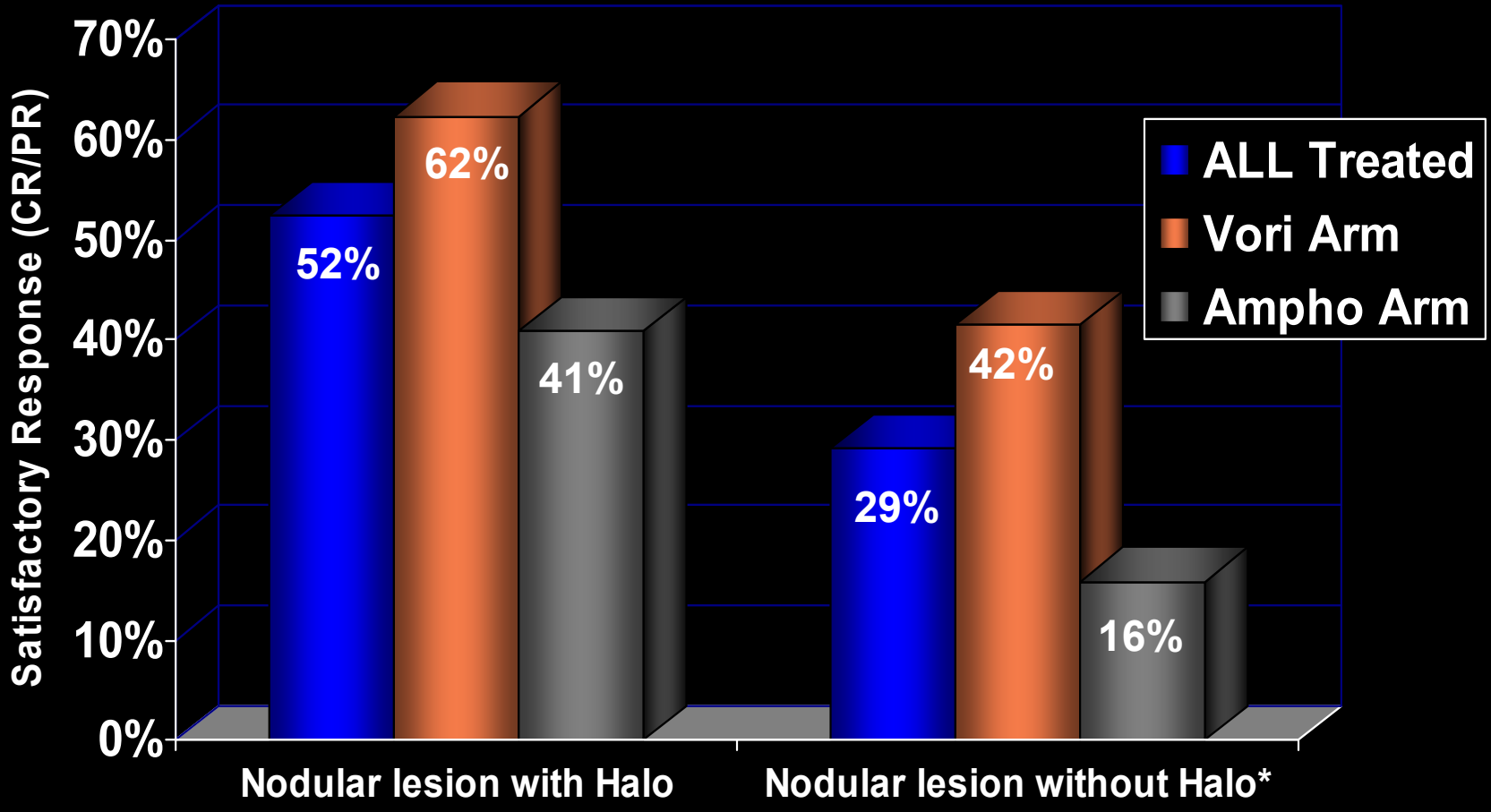
Herbrecht R et al *NEJM* 2002;347:408-15; Patterson TF et al. *Clin Infect Dis* 2005;41:1448-52; Greene RE et al. *Clin Infect Dis* 2007;44:373-9

S ◆ A ◆ C ◆ M ◆ M
San Antonio Center for Medical Mycology

Voriconazole: Important Considerations

- Watch for drug interactions
- Significant adverse events: hepatic, visual, rash
- IV formulation: accumulation of cyclodextrin in renal insufficiency
- Potential for azole cross-resistance
- No activity versus Zygomycetes
- Consideration for weight-based oral therapy/measurement of serum levels

Patients with Satisfactory Treatment Response Categorized by Baseline CT Findings



*Note: Required positive mycology

Greene RE et al. *Clin Infect Dis* 2007;44:373-9

S ◆ A ◆ C ◆ M ◆ M
San Antonio Center for Medical Mycology

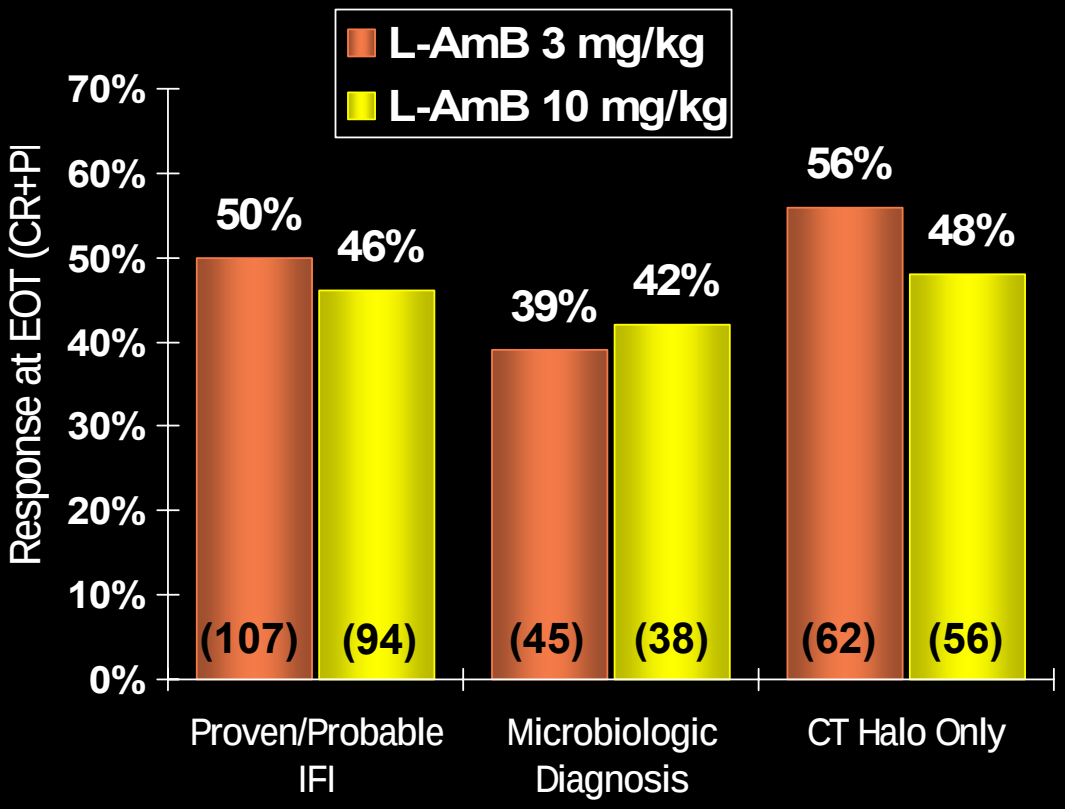
The Strategy of Following Voriconazole (Vori) or Amphotericin B (AmB) with Other Licensed Antifungal Therapy (OLAT)

Category/Reason for switch	Success at wk 12 (%)	
	Vori (n=144)	AmB (n=133)
Overall success	76/144 (53)	42/133 (32)
Received OLAT	25/52 (48%)	41/107 (38%)
Intolerance (adverse event, lab abnormality)	8/19 (42)	27/74 (36)
Insufficient clinical response	5/16 (31)	4/19 (21)
Completed therapy and received OLAT	11/14 (79)	6/10 (60)
Other	1/3	4/4

- Pts switched to lipid formulations of AmB following initial AmB had success in 14/47 (30%)

Herbrecht R et al. *NEJM* 2002;347:408-15;
Patterson TF et al. *Clin Infect Dis* 2005;41:1448-52

Efficacy of Liposomal AmB (L-AmB) in Invasive Mycoses: AmBiLoad Trial



- 14 day loading dose of L-AmB 3 or 10 mg/kg/d followed by L-AmB 3 mg/kg/d

	L-AmB 3	L-AmB 10
IPA	96%	97%
CT Halo	58	60
Allo-SCT	16	19
Neutropenia	71	76
Survival	72	59
Toxicity	20	32

Note: L-AmB=liposomal amphotericin B; CR+PR=complete & partial responses; EOT=End of Therapy; IPA=invasive pulmonary aspergillosis; Allo-SCT=allogeneic stem cell transplant

Cornely OA et al. *Clin Infect Dis* 2007;44:1289-97

S ◆ A ◆ C ◆ M ◆ M
San Antonio Center for Medical Mycology

Efficacy and Safety of Liposomal Amphotericin B and Amphotericin B lipid Complex in Invasive Pulmonary Aspergillosis (IPA)

Therapy phase	No. of patients (%) High dose	Low dose	*P*
Primary therapy			
L-AMB			
Response*	2/18 (11)	5/39 (13)	.99
AE	2/36 (5.5)	5/70 (7)	.66
ABLC			
Response*	1/5 (20)	3/29 (10)	.49
AE	1/7 (14.3)	5/45 (11)	.49
Salvage therapy			
L-AMB			
Response*	3/21 (14)	1/13 (8)	.99
AE	12/34 (35)	3/17 (18)	.19
ABLC			
Response*	1/13 (8)	1/5 (20)	.49
AE	7/18 (39)	2/12 (17)	.25

L-AMB indicates liposomal amphotericin B; AE indicates AE, adverse event; ABLC, amphotericin B lipid complex.
* Response in patients who received ≥7 days of therapy.

- Retrospective study of 381 patients with hematological malignancy
- Documented IPA
- Poor primary and salvage responses (8-16%) with either high (≥7.5 mg/kg/d) or low (5-7.5 mg/kg/d) doses of lipid formulations of amphotericin B

Hachem RY, et al *Cancer* ePub 25 Jan., 2008

S ◆ A ◆ C ◆ M ◆ M
San Antonio Center for Medical Mycology

Key Recommendation:
Salvage Therapy

For salvage therapy, agents include lipid formulations of amphotericin (AII), posaconazole (BII), itraconazole (BII) or caspofungin (BII).

Salvage therapy for invasive aspergillosis poses important challenges with significant gaps in knowledge.

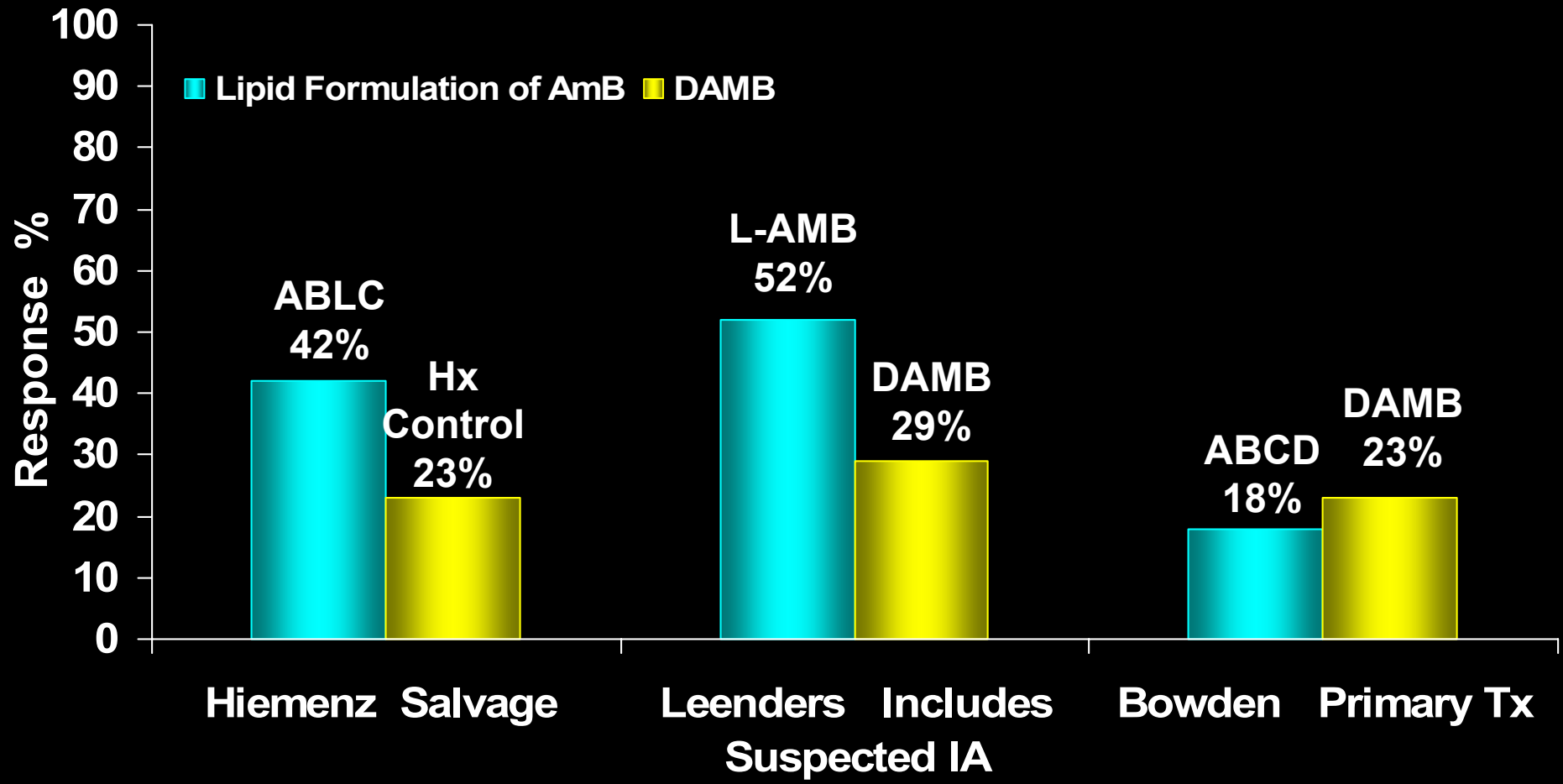
Key Recommendation: Salvage Therapy

- Assessment of patients with refractory aspergillosis may be difficult. In evaluating such patients:
  - The diagnosis of invasive aspergillosis should be established if it was previously uncertain and should be confirmed if it was previously known.
  - The drug dosage should be considered.
  - Management options include a change to intravenous therapy and therapeutic monitoring of drug levels.

Key Recommendation: Salvage Therapy

- In patients whose aspergillosis is refractory to voriconazole, a paucity of data exists to guide management.
  - Therapeutic options include a change of class using an amphotericin B (AMB) formulation or an echinocandin such as caspofungin (BII)
  - Refractory infection may respond to a change to another drug class (BII) or to a combination of agents (BII).

Polyene Therapy for Invasive Aspergillosis



Hiemenz JW et al. *Blood* 1995;86(suppl 1):849a; Leenders ACAP et al. *Br J Haem* 1998;103:205; Bowden RA et al. *Clin Infect Dis* 2002;35:359-66.

S ◆ A ◆ C ◆ M ◆ M
San Antonio Center for Medical Mycology

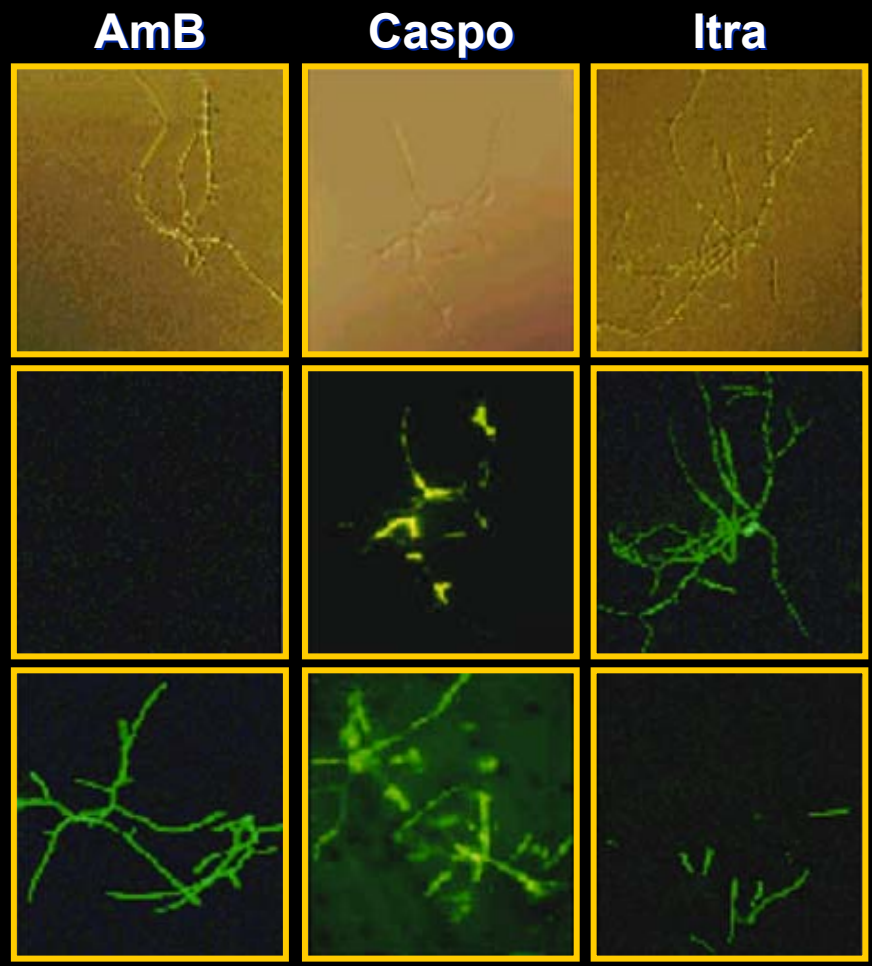
In Vitro & Clinical Activity of Echinocandins on *Aspergillus*

In vitro activity:

- Not classically fungicidal or fungistatic
- Activity against other *Aspergillus* spp. (*A terreus*)
- Animal models prolonged survival

Clinical efficacy:

- Salvage therapy: ~40% efficacy in pts with progressive infection
- Primary therapy: limited activity (~33%)
- Excellent tolerability
- Role in combination therapy

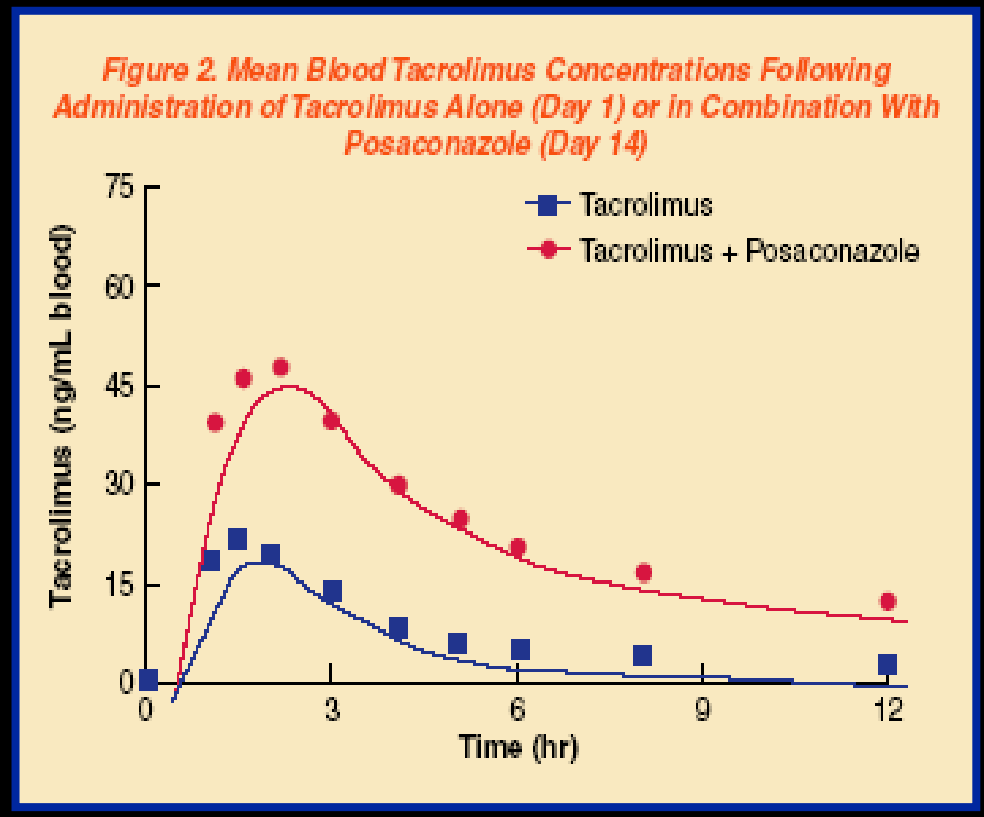


Bowman et al. *Antimicrobial Agents Chemother* 2002;46:3001-3012; Maertens J, et al. *Clin Infect Dis* 2004;39:1563-71; Kirkpatrick WR, et al. *Antimicrob Agents Chemother* 2002; 46: 2564-8; Viscoli C, et al. TIMM 2008

S ◆ A ◆ C ◆ M ◆ M
San Antonio Center for Medical Mycology

Extended Spectrum Triazoles: Posaconazole

- Broad spectrum (Zygomycetes)
- Oral (no IV) linear to 800 mg
- Posaconazole absorption increased by food
  - Saturable absorption
- Posaconazole metabolized minimally by glucuronidation
- Posaconazole inhibits CYP3A4
  - Potential interaction with many other drugs such as tacrolimus
  - Increase in catabolism from rifampin – stimulates glucuronidase – posaconazole levels reduced dramatically



Sansone-Parsons A. *Antimicrob Agents Chemother* 2006;50:1881; Dodds Ashley ES et al. *Clin Infect Dis* 2006;43:S28-39; Sansone A et al *ICAAC 2003* (abstract A-1603)

S ◆ A ◆ C ◆ M ◆ M
San Antonio Center for Medical Mycology

Posaconazole Salvage Therapy for Invasive Aspergillosis

- Open, salvage therapy; historical controls refractory or intolerant of standard therapy
- Posaconazole: Oral solution (200mg qid X2 wk/400mg bid)

Aspergillus species	Posaconazole (n)	Historical Controls (n)
All *Aspergillus*	42% (107)	26% (86)
A. fumigatus	41% (29)	35% (34)
A. flavus	53% (19)	19% (16)
A. terreus	29% (14)	18% (11)

- Adverse events: 4-10% (Headache, abdominal pain, nausea, liver enzyme elevations)
- Better responses with higher drug levels

Walsh TJ, et al. *Clin Infect Dis* 2007;44:2-12

S ◆ A ◆ C ◆ M ◆ M
San Antonio Center for Medical Mycology

Key Recommendations: Extrapulmonary Infection

Preferred therapy: Although the preponderance of cases treated with voriconazole consisted of invasive pulmonary aspergillosis (IPA), other cases of extrapulmonary and disseminated infection allow one to infer that voriconazole is effective in these cases.

- Case series:
  - Bone infection: Complete/Partial responses: 11/20 (55%)
  - Central nervous system: 81 pts; responses in 35% (vs <10% historical data)
- Anecdotal success:
  - Keratitis, endophthalmitis, endocarditis, etc.

Schwartz S, et al. Blood 2005;106:2641-5; Mouas H, et al. *Clin Infect Dis* 2005;40:1141-7

S ◆ A ◆ C ◆ M ◆ M
San Antonio Center for Medical Mycology

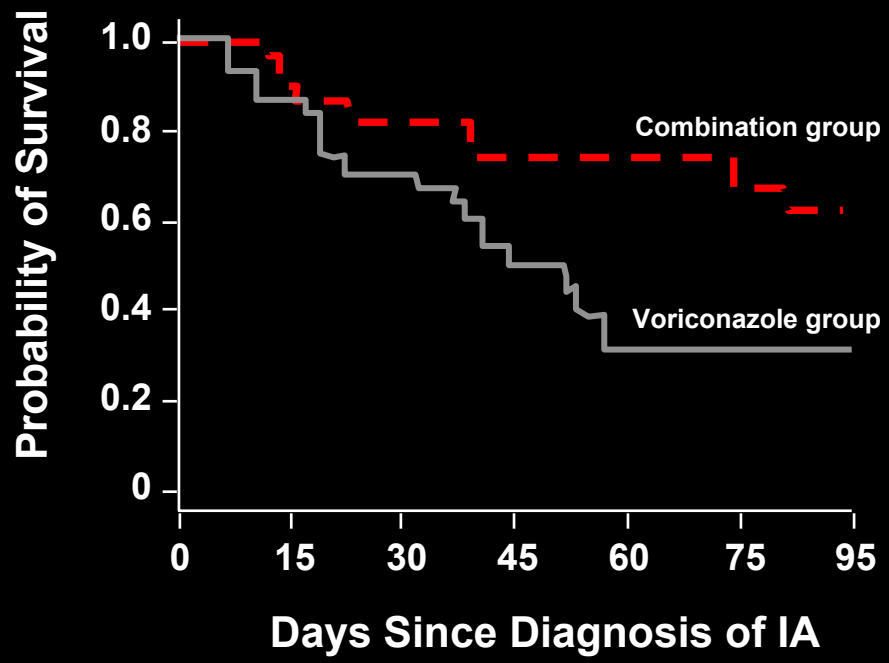
Key Recommendations: Combination Therapy

In the absence of a well-controlled prospective clinical trial, routine initial administration of combination therapy is not recommended (BII).

However, that in the setting of salvage therapy, an additional antifungal agent might be added to current therapy, or combination antifungal drugs from different classes other than the initial regimen may be used (BII).

Combination Therapy for Invasive Aspergillosis

- In vitro
  - Most interactions show synergy / additive effects (Perea, 2002)
  - Some combinations antagonistic (Meletiadis, 2006)
  - Poor correlation between in vitro results and in vitro efficacy (Johnson, 2004)
- Experimental infections
  - Candin plus polyene (Kohno, 2000; Nakajima, 2000)
  - Candin plus azole (Kirkpatrick, 2002; Petraitiene, 2002)
    - Improved sterilization of tissues
    - Reduced tissue burden
- Anecdotal clinical series
  - Candin+polyene (Aliff, 2003; Kontoyiannis, 2003; Denning, 2006)
  - Candid plus azole (Marr, 2004; Maertens, 2006; Singh, 2006)



S ◆ A ◆ C ◆ M ◆ M
San Antonio Center for Medical Mycology

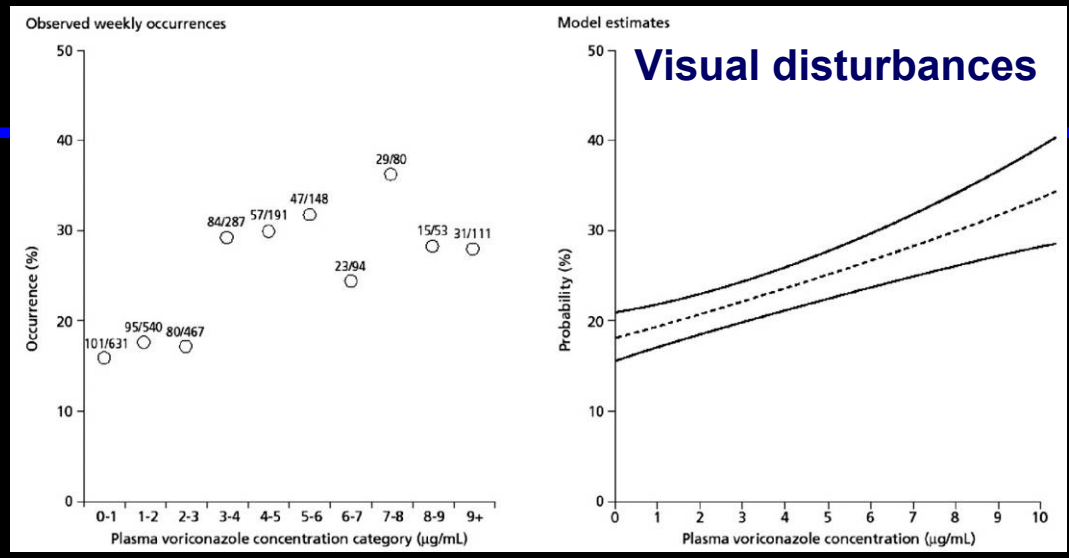
Key Recommendations: Role of Therapeutic Drug Monitoring

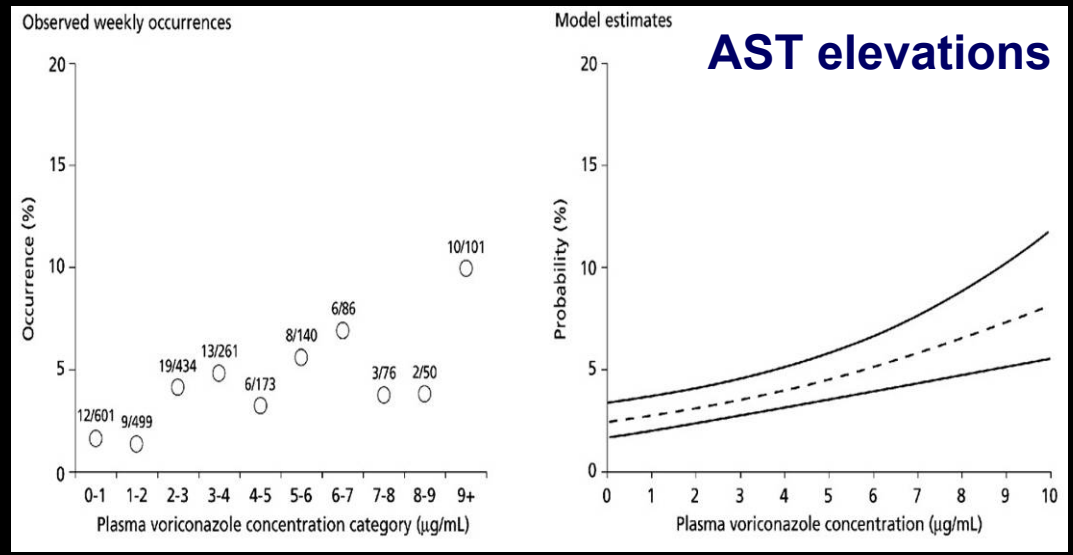
Although further work is needed to validate therapeutic drug monitoring (TDM) approaches for antifungals, the committee recommends that determination of a plasma drug level, in conjunction with other measures of clinical assessment, may be another factor in evaluating reasons for therapeutic failure due to sub-optimal drug exposures or for toxicity due to the drug (BIII).

S ◆ A ◆ C ◆ M ◆ M
San Antonio Center for Medical Mycology

Voriconazole Serum Concentrations & Adverse Events

- Correlation between adverse events and plasma concentrations
- Plasma voriconazole concentrations >6 µg/ml associated with increased toxicity
  - Visual events: ~25-35%
  - Liver abnormalities: ~8-15%
- No cut-off level predictive of adverse event





Tan K et al. *J Clin Pharmacol*. 2006;46:235-43.

S • A • C • M • M
San Antonio Center for Medical Mycology

Measurement of Voriconazole Serum Concentrations

- Potential reasons to monitor include:
  - Nonlinear kinetic profile
  - Dependence on CYP2C19
  - Extensive metabolizers with 2- to 4-fold lower exposure than heterozygous & poor metabolizers
  - High inter-patient variability
- Prior studies failed to detect relationship between outcome and concentrations
  - Trend for lower responses with random levels <0.5 µg/ml
- Levels in hematopoietic stem cell transplantation (HSCT) undetectable in 15%

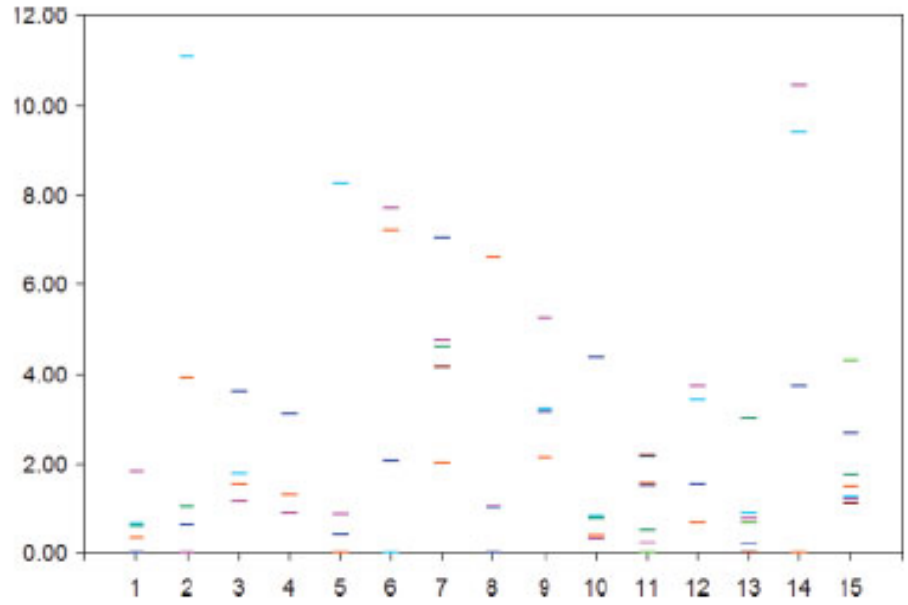
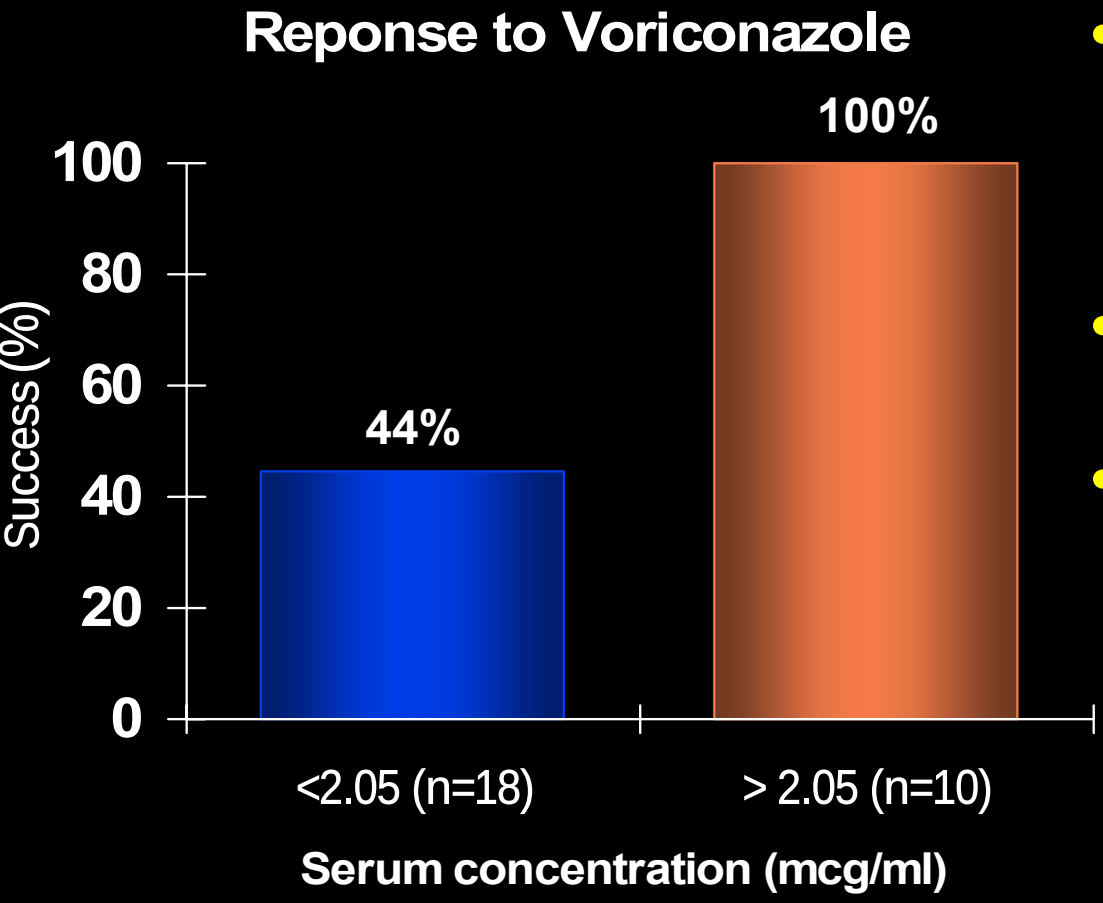


FIGURE 2. Voriconazole levels in 15 patients in whom ≥4 values were available illustrating variability.

Lutsar I et a. *Clin Infect Dis* 2003,36:1087-93; Trifilio S et al. *Cancer* 2007;109:1532-5

S ◆ A ◆ C ◆ M ◆ M
San Antonio Center for Medical Mycology

Therapeutic Drug Monitoring: Voriconazole Serum Concentration and Response



- Random voriconazole levels in patients with progression (n=17) or toxicity (n=11)
- Better responses in patients with higher levels
- Improved outcomes with dose escalation in patients with levels < 2 mcg/ml

Smith J et al. *Antimicrob Agents Chemother* 2006;50:1570-2

S ◆ A ◆ C ◆ M ◆ M
San Antonio Center for Medical Mycology

Posaconazole Plasma Concentrations and Global Response in Invasive Aspergillosis

Quartile	No. of subjects*	Plasma C_{max}		Plasma C_{avg}		No. (%) of responders
		Mean ng/mL	CV (%)	Mean ng/mL	CV (%)	
1	17	142	51	134	45	4 (24)
2	17	467	27	411	21	9 (53)
3	17	852	15	719	12	9 (53)
4	16	1480	16	1250	28	12 (75)

Issues for consideration:

- Doses higher than 800 mg/d do not increase plasma concentrations
- Lack of IV formulation prolongs time to steady state levels (~7days)
- Measurement of levels not widely available; higher doses unlikely to increase levels.

Walsh TJ, et al. *Clin Infect Dis* 2007;44:2-12

S ◆ A ◆ C ◆ M ◆ M
San Antonio Center for Medical Mycology

Key Recommendations: Antifungal Prophylaxis

Antifungal prophylaxis with posaconazole can be recommended in the subgroup of HSCT recipients with graft versus host disease (GVHD) at high risk for IA and in neutropenic patients with acute myelogenous leukemia or myelodysplastic syndrome who are at high risk for IA (AI).

Antifungal Prophylaxis for Moulds

- Amphotericin B
  - Intravenous (dose-limiting toxicity, lower doses not effective)
  - Intranasal/aerosol (limited delivery, poor tolerability)
- Azoles
  - Fluconazole (lack of efficacy for moulds)
  - Itraconazole (erratic bioavailability, toxicity)
- New agents—potential activity
  - Echinocandins (intravenous, daily/cost, spectrum)
  - Newer azoles: posaconazole; voriconazole, investigational (bioavailability, spectrum of activity, potential for resistance, drug interactions)
  - Inhaled amphotericin (improved delivery, efficacy)

MMWR, 2000;49(RR-10):64; Winston DJ et al, *Transplantation* 2002;74:688-95; Palmer SM et al, *Transplantation* 2001;72:545-8; Van Burik J et al, *Clin Infect Dis* 2004;36:1407-16; Ullmann AJ, et al. *NEJM* 2007;356:335-47; Cornely OA et al. *NEJM* 2007;356:348-59; Wingard JR, ASH 2007 (abstract 163)

Posaconazole vs Fluconazole for Prophylaxis of Invasive Fungal Infections in HSCT recipients with GvHD

Proven/Probable IFI (EORTC/MSG definitions)	Posaconazole (200 mg tid) n=301	Fluconazole (400 mg qd) n=299
At any time	20 (7%) p=.003	42 (14%)
Study period (16 wks)		
Total	16 (5%) p=.07	27 (9%)
Aspergillus	7 (2%) p=.004	21 (7%)
Breakthrough (on therapy)		
Total	7 (2%) p=.004	22 (8%)
Aspergillus	3 (1%) p=.001	17 (6%)

Ullmann AJ, et al. *NEJM* 2007;356:335-47

Posaconazole vs Standard of Care (Fluconazole [Flu] or Itraconazole [Itra]) for Prophylaxis of Invasive Fungal Infection (IFI) with in Patients with Acute Myelogenous Leukemia or Myelodysplastic Syndrome

Endpoint	Posaconazole (200 mg tid) n=304	Flu (400 mg qd)/Itra (200 mg bid) n=298
IFI during treatment	7 (2%) p=.0009	25 (8%)
Aspergillosis	2 (1%) p=.0001	20 (7%)
IFI at Day 100	14 (5%) p=.0031	33 (11%)
Deaths attributed to IFI	5 (2%) p=.012	16 (5%)
Deaths to d100	44 (14%) p=.025	64 (21%)
Adverse events	102 (34%)	71 (30%)/30 (52%)

Cornely OA et al. *NEJM* 2007;356:348-59

S • A • C • M • M
San Antonio Center for Medical Mycology

Role of Posaconazole Prophylaxis in High Risk Patients with AML and HSCT

- Heterogeneity of risk
  - Rates of aspergillosis in acute leukemia: 2-28%
  - Less benefit in populations at lower risk
- Prolonged period of risk
  - Less than 1/3 neutropenic at time of diagnosis
  - Risk after 40 days: age, underlying disease, GVHD, steroid use
  - Late infection (90 to >180 days) increasingly common
- Utility of antigen testing (detection of early infection):

Galactomannan at baseline	Rate of IFI in GVHD (%)	
	Posaconazole	Fluconazole
Positive	2/21 (10%)	7/30 (23%)
Negative	12/259 (5%)	20/243 (8%)

- Other populations (lung transplant, etc.) not studied

Wald A, et al. *J Infect Dis* 1997;175:1459-66; De Pauw BE, *NEJM* 2007; 356:409; Ullmann AJ, et al. *NEJM* 2007;356:335-47; Cornely OA et al. *NEJM* 2007;356:348-59

Voriconazole Prophylaxis: Allogeneic SCT (2003-2006)

- Prospective, randomized, double-blind trial (600 patients)
- Duration day 0 → days +100/+180
- Serum GM twice weekly x 60 days, once to twice weekly until day +100
- Both arms similar in
  - Patient, disease type, transplant type, engraftment rate
  - Acute/chronic GVHD, non-fungal infection, study withdrawal
- IFI: 25 proven, 30 probable, 15 presumptive, 74 possible
  - Proven/probable/presumptive IFI similar in 2 arms
  - 6 months: voriconazole 6.6%, fluconazole 10.6%; 12 months: voriconazole 11.6%, fluconazole 13.1%
  - *Aspergillus:* voriconazole 7, fluconazole 16 (*P*=.05); *Candida* 3 and 3, *Zygomycetes* 2 and 3
- Fungal-free survival at 6 months: voriconazole 78%, fluconazole 76%
- Event-free/overall survival similar
- Conclusion: Efficacies of voriconazole and fluconazole are similar with close monitoring and early therapy

Wingard JR. 49th Am Soc Hematology Ann Mtg; 2007; Abstract #163.

S ◆ A ◆ C ◆ M ◆ M
San Antonio Center for Medical Mycology

Key Recommendations:
Chronic, Saprophytic, & Allergic Conditions

Condition	Preferred therapy	Alternative Agents	Comments
Chronic necrotizing pulmonary aspergillosis	Similar to invasive pulmonary aspergillosis	Similar to invasive pulmonary aspergillosis (IPA)	Long course of therapy (mos); oral triazole preferred over a parenterally agent
Aspergilloma	No therapy or surgical resection	Itraconazole or voriconazole; similar to IPA	The role of medical therapy in aspergilloma is uncertain.
Chronic cavitary pulmonary aspergillosis	Itraconazole or voriconazole	Similar to IPA	Long-term therapy may be needed. Surgical resection may lead to complications.
Allergic bronchopulmonary aspergillosis	Itraconazole	Voriconazole or posaconazole	Itraconazole has corticosteroid sparing effect.
Allergic *Aspergillus* sinusitis	None or itraconazole	Little data on other agents	

Guidelines for Treatment of Invasive Aspergillosis

- Importance of early detection
  - Role of radiological diagnosis
  - Non-culture based diagnostics [galactomannan & (1→3)-β-D-glucans]
    - Importance of serial samples
    - Impact of prior therapy
  - Poorer outcomes with extensive or disseminated disease
- Limited efficacy of amphotericin B deoxycholate in high risk pts
- Recommendations for treatment of invasive aspergillosis
  - Voriconazole as primary therapy in most patients
  - Liposomal amphotericin alterative therapy in some patients
  - Options for salvage therapy; dependent on prior therapy, host factors, dosing considerations; potential agents: posaconazole, itraconazole, echinocandins, lipid amphotericin formulations
  - Clinical trials needed for combination therapy
- Prophylaxis with posaconazole prophylaxis can be recommended in high risk patients

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

S ◆ A ◆ C ◆ M ◆ M
San Antonio Center for Medical Mycology

Acknowledgements

IDSA *Aspergillus* Guidelines Committee

- T.J. Walsh, Co-Chair
- T.F. Patterson, Co-Chair
- E.J. Anaissie
- D.W. Denning
- R. Herbrecht
- D.P. Kontoyiannis
- K.A. Marr
- V.A. Morrison
- B.H. Segal
- W.J. Steinbach
- D.A. Stevens
- J-A van Burik
- J.R. Wingard
- T. M. File, Jr.: IDSA Standards and Practice Guidelines Committee
- J. Padberg, IDSA Staff Support

S ◆ A ◆ C ◆ M ◆ M

San Antonio Center for Medical Mycology

Thank you!

Want to know more?

www.doctorfungus.org

S ◆ A ◆ C ◆ M ◆ M

San Antonio Center for Medical Mycology