IMMi

Relevanz der Empfindlichkeitsprüfung für die Therapie

Peter-Michael Rath

Interessenkonflikte: keine

Institut für Medizinische Mikrobiologie
Universitätsklinikum Essen

pm.rath@uni-due.de

Universitätsklinikum Essen

90-60-Regel in der Bakteriologie

Mit einen in-vitro wirksamen Medikament werden 90% der Patienten gesund.

Mit einem in-vitro unwirksamen Medikament werden 60% der Patienten gesund.

Bakteriologie

Table 1. The "90-60 rule": the range of correlations between susceptibility and outcome in studies of bacterial infections.

Reference	Type(s) of infection	Drug(s) administered	Outcome measurement	Measurement used to determine susceptibility	Cases with successful outcome, % (no. of cases/ total no. of cases), by susceptibility class		P
					Susceptible[a]	Resistant	
[11]	Bacteremia and fungemia	Various	Mortality	MIC[b]	73 (224/309)	48 (10/21)	.02
[12]	Bacteremia and fungemia	Various	Mortality	MIC[b]	89 (594/665)	77 (97/126)	<.001
[10]	Serious bacterial infections	Various	Clinical response	MIC	81 (219/271)	4 (1/27)	<.001
[13]	Pneumococcal otitis media	Amoxicillin/clavulanic acid	Clinical response	MIC	80 (149/186)	68 (15/23)	.26
[14]	Pneumococcal otitis media	Cefuroxime	Clinical response	MIC	94 (44/47)	78 (29/37)	.05
[15]	Pneumococcal otitis media[c]	Cefaclor or cefuroxime	Bacteriologic response	MIC	95 (55/58)	45 (9/20)	<.001
[16]	Pneumococcal otitis media[c]	Cefaclor or azithromycin	Bacteriologic response	MIC	89 (23/26)	24 (6/25)	<.001
[17]	*Bacteroides* bacteremia	Various	Bacteriologic response	MIC	88 (60/68)	57 (4/7)	.06
[18]	Moderate-to-severe bacterial infections	Ciprofloxacin	Bacteriologic response	AUC/MIC ratio	82 (37/45)	26 (5/19)	<.001
[19]	Bacterial infections	Aminoglycosides	Clinical response	Peak/MIC ratio	~90[d]	~55[d]	
[3]	Bacterial infections[e]	Cefotaxime	Bacteriologic response	Zone diameter	92 (1464/1591)	63 (31/49)	<.001
[3]	Bacterial infections[e]	Ciprofloxacin	Bacteriologic response	Zone diameter	91 (1652/1815)	62 (8/13)	.004
Total	—	—	—	—	89 (4521/5081)	59 (215/366)	<.001

89 % **59 %**

Mykologie - Fluconazol

Table 3. Range of correlations of susceptibility testing with outcome for fungal infections

Reference	Type(s) of infection	Drug administered, dosage in mg/day	Outcome measurement	MIC used to determine susceptibility, μg/mL	Cases with successful outcome, % (no. of cases/ total no. of cases), by susceptibility class		P
					Susceptible	Resistant	
[5]	Candidiasis, mostly mucosal	Fluconazole, 100	Clinical response	≤8	98 (248/253)	76 (37/49)	<.001
[31]	Mucosal candidiasis	Fluconazole, 100–200	Clinical response	MIC relative to dose	80 (28/35)	46 (6/13)	.034
[32]	Mucosal candidiasis	Fluconazole, 100	Clinical response	≤8	96 (49/51)	0 (0/15)	<.001
[33]	Mucosal candidiasis	Fluconazole, 100–400	Clinical response	≤32	88 (14/16)	0 (0/5)	.001
[5]	Mucosal candidiasis	Itraconazole, 200	Clinical response	≤0.125	88 (162/184)	59 (47/80)	<.001
[32]	Mucosal candidiasis	Itraconazole, 200	Clinical response	≤0.5	98 (48/49)	6 (1/17)	<.001
[32]	Mucosal candidiasis	Ketoconazole, 400	Clinical response	<0.125	94 (46/49)	11 (2/18)	<.001
[33]	Mucosal candidiasis	Ketoconazole, ~400	Clinical response	<0.06	94 (17/18)	0 (0/3)	.003
[5]	Candidiasis, mostly invasive	Fluconazole, >100; median, 400	Clinical response	≤32	82 (146/178)	46 (18/39)	<.001
[28]	Invasive candidal infections	Fluconazole, 400	Clinical response	≤32	77 (23/30)	0 (0/2)	.073
[29]	Candidemia	Fluconazole, mostly 100–200	Clinical response	<8	52[a]	<14[a]	.03
[46]	Cryptococcal meningitis	Fluconazole, ~400	Clinical response	<16	91 (21/23)	0 (0/5)	<.001
[52]	Disseminated histoplasmosis	Fluconazole, 600–800	Clinical response	<5	97 (36/37)	71 (20/28)	.004
Total	—	—	—	—	91 (838/923)	48 (131/274)	<.001

NOTE. All MICs were determined by NCCLS M27-A [8] or a closely related variant of that method. *P* values determined by Fisher's exact test.

[a] Published data do not provide additional detail.

91 % **48 %**

Fluconazol: Dosis/MHK-Ratio

Table 2
Daily dose of fluconazole likely to be effective against *Candida* based on MIC*

Daily dose	MIC
100 mg	≤4 μg/mL
200 mg	≤8 μg/mL
400 mg	≤16 μg/mL
800 mg	≤32 μg/mL

* Assumptions: AUC/MIC ≥25 should be effective. Daily dose of fluconazole approximates AUC in average size patient with normal renal function.

TABLE 6. Relationship between dose/MIC ratio and clinical response in fluconazole treatment of mucosal and invasive candidiasis

Dose/MIC	% Clinical success (*n*/*N*)[a]				
	Rex et al. (85)[b]	Clancy et al. (18)[c]	Lee et al. (38)[c]	Takakura et al. (100)[c]	Total
≥400	99 (115/116)	89 (8/9)			98 (123/125)
100–300	98 (129/132)	60 (6/10)			95 (135/142)
50–75	92 (34/37)	0 (0/1)	79 (19/24)		86 (53/62)
25–37.5	91 (30/33)	0 (0/1)	67 (4/6)	70 (144/206)	72 (178/246)
6.26–12.5	74 (35/47)	20 (1/5)		64 (16/25)	68 (52/77)
<6.25	65 (30/46)	0 (0/6)	0 (0/2)	55 (6/11)	55 (36/65)

[a] Abbreviations: *n*, number of successful treatment events; *N*, number of total patient-episode-isolate events.
[b] Mucosal infection study.
[c] Invasive candidiasis (candidemia) study.

CLINICAL MICROBIOLOGY REVIEWS, Apr. 2006, p. 435–447

D.R. Hospenthal et al. / Diagnostic Microbiology and Infectious Disease 48 (2004) 153–160

Correlation of MIC with Outcome for *Candida* Species Tested against Voriconazole: Analysis and Proposal for Interpretive Breakpoints

M. A. Pfaller,[1]* D. J. Diekema,[1] J. H. Rex,[2] A. Espinel-Ingroff,[3] E. M. Johnson,[4] D. Andes,[5]

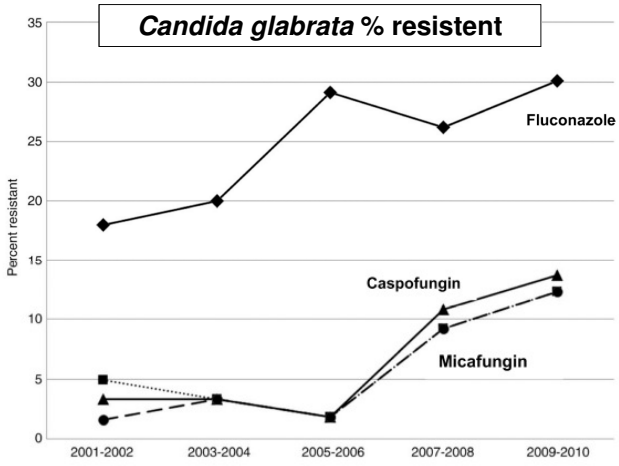
TABLE 4. Investigator assessment of efficacy versus baseline MIC for *Candida* species in primary and salvage therapy studies 603, 608, 309/604, and 301/606

MIC breakpoint (μg/ml)	Interpretive category	No. of isolates	% Success
≤0.25	S	189	77
0.5–2	SDD	39	54
≥4	R	21	62
≤0.5	S	211	73
1–2	SDD	17	65
≥4	R	21	62
≤1	S	221	74
2	SDD	7	43
≥4	R	21	62

JOURNAL OF CLINICAL MICROBIOLOGY, Mar. 2006, p. 819–826

Echinocandin Resistance, Susceptibility Testing and Prophylaxis: Implications for Patient Management

David S. Perlin,



Mutationen in FSK 1 / 2 hot spots

Fig 1.
Temporal trends in antifungal resistance of *Candida glabrata* isolates to fluconazole, anidulafungin, caspofungin, and micafungin. Adapted from Alexander et al. [59]

Drugs. 2014 September ; 74(14): 1573–1585

Echinocandin resistance and population structure of invasive *Candida glabrata* isolates from two university hospitals in Germany and Austria

Ulrike Klotz,[1] Dirk Schmidt,[1] Birgit Willinger,[2] Eike Steinmann,[3] Jan Buer,[1] Peter-Michael Rath[1] and Joerg Steinmann[1]

Table 1 Antifungal susceptibility testing of 64 *C. glabrata* isolates by EUCAST broth microdilution method.

Antifungal agent	MIC (mg l^{-1}) Range	MIC_{50}	MIC_{90}	Susceptible *n* (%)	Intermediate *n* (%)	Resistant *n* (%)
AMB	0.125–0.25	0.25	0.5	64 (100)	0	0
FLC	4–128	16	128	0	48 (75)	16 (25)
VRC	0.03–16	0.5	4	45 (70)[1]	NA[2]	19 (30)[1]
AND	0.03–2	0.06	0.06	63 (98)	0	1 (1.6)
CAS	0.016–16	0.03	0.06	63 (98)[3]	NA[2]	1 (1.6)[3]
MCF	0.016–1	0.016	0.016	63 (98)	0	1 (1.6)

AMB, amphotericin B; FLC, fluconazole; VRC, voriconazole; AND, anidulafungin; CAS, caspofungin; MCF, micafungin.
[1]According to Posteraro *et al.* [21].
[2]Not available.
[3]According to CLSI [22].

S663P in FKS2 Gen hot spot 1

Mycoses, 2016, **59**, 312–318

Abhängigkeit von Testmethode

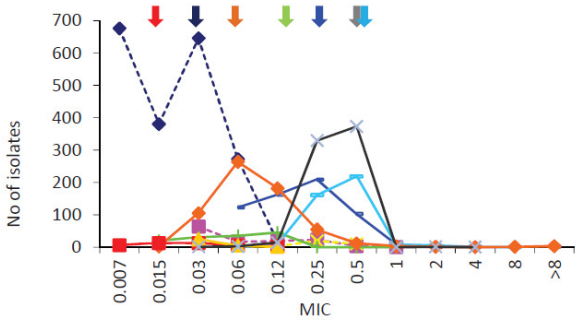


Fig 9. Diagram showing the individual caspofungin MIC distributions for *C. albicans* obtained at nine reference laboratories in Europe and the US. Three dataset were generated using the CLSI method (dotted lines) and with peaks at ≤ 0.07 and 0.03 mg/L (blue) or ≤ 0.03 mg/L (magenta and yellow). Seven dataset were generated using the EUCAST methodology (solid lines) and with peaks of the distributions at various concentrations between 0.06 and 0.5 mg/L. Obviously, it is not possible to combine such divergent datasets and select a meaningful ECOFF. (Arrows indicate the individual peaks of the distributions, marked by the colour corresponding to the dataset in question).

C. albicans

9 Referenzlabore

3 x CLSI

7 x EUCAST

Kein ECOFF
(epidemiologischer cutoff)
möglich !

Maiken Cavling Arendrup Dan Med J 2013; 60(11): B4698

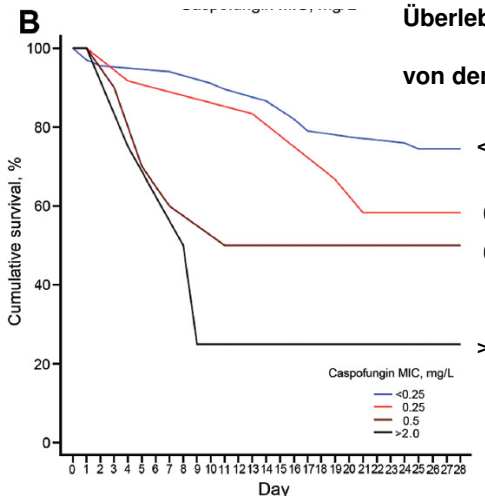
EUCAST Grenzwerte *Candida*

Antifungal agent	MIC breakpoint (mg/L)													
	C. albicans		*C. glabrata*		*C. krusei*		*C. parapsilosis*		*C. tropicalis*		*C. guilliermondii*		Non-species related breakpoints[1]	
	S ≤	R >	S ≤	R >	S ≤	R >	S ≤	R >	S ≤	R >	S ≤	R >	S ≤	R >
Amphotericin B	1	1	1	1	1	1	1	1	1	1	IE	IE	IE	IE
Anidulafungin	0.032	0.032	0.064	0.064	0.064	0.064	0.002	4	0.064	0.064	IE[2]	IE[2]	IE	IE
Caspofungin	Note[3]	Note[3]	Note[3]	Note[3]	Note[3]	Note[3]	Note[3]	Note[3]	Note[3]	Note[3]	IE[2]	IE[2]	IE	IE
Fluconazole	2	4	0.002	32	-	-	2	4	2	4	IE[2]	IE[2]	2	4
Isavuconazole	IE	IE	IE	IE	IE	IE	IE	IE	IE	IE	IE	IE	IE	IE
Itraconazole	0.064	0.064	IE[2]	IE[2]	IE[2]	IE[2]	0.125	0.125	0.125	0.125	IE[2]	IE[2]	IE	IE
Micafungin	0.016	0.016	0.032	0.032	IE[4]	IE[4]	0.002	2	IE[4]	IE[4]	IE[4]	IE[4]	IE	IE
Posaconazole	0.064	0.064	IE[2]	IE[2]	IE[2]	IE[2]	0.064	0.064	0.064	0.064	IE[2]	IE[2]	IE	IE
Voriconazole	0.125[5]	0.125[5]	IE	IE	IE	IE	0.125[5]	0.125[5]	0.125[5]	0.125[5]	IE[2]	IE[2]	IE	IE

EUCAST Antifungal Clinical Breakpoint Table v. 8.1 valid from 2017-03-01

Drug-Resistant *Candida glabrata* Infection in Cancer Patients

Dimitrios Farmakiotis,[1] Jeffrey J. Tarrand, and Dimitrios P. Kontoyiannis



Überleben in Abhängigkeit von der Caspofungin-MHK

< 0.25 (17/67)

0.25 (5/12)

0.5 (5/10)

> 2.0 (3/4)

Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 20, No. 11, November 2014

Probleme bei systemischen Hyphomyzeten-Infektionen

Erreger	**Resistente Erreger waren bislang selten**
	Standardisierung der Resistenztestung erst kürzlich
	Resistenztestungen werden nicht überall durchgeführt
Medikamente	**Wirkungsmechanismus zum Teil unklar (Amphotericin B)**
	Keine einfache Dosis-/Konzentrationsbeziehung
	Variable Pharmakokinetik und -dynamik
Patienten	Relativ seltene Erkrankung
	Relativ hohe Letalität durch Grunderkrankung
	Diagnosekriterien waren lange Zeit uneinheitlich
	Wenige gesicherte Infektionen
	Infektionsdiagnose spät

Therapeutic drug monitoring of voriconazole helps to decrease the percentage of patients with off-target trough serum levels

Jesús Guinea[1,2,3,4,*], Pilar Escribano[1,2,3],

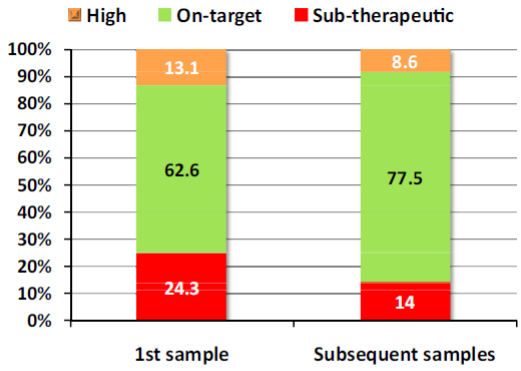


FIGURE 1. Proportion of first and subsequent samples with sub-therapeutic, on-target, and high voriconazole levels. This Figure is reproduced in color in the online version of *Medical Mycology*.

Talspiegel

< ~ 1mg/l: vermehrt Therapieversagen

> ~ 5 mg/l: vermehrt Toxizität

Medical Mycology, 2016, 0, 1–8
doi: 10.1093/mmy/myv099

Probleme bei systemischen Hyphomyzeten-Infektionen

Erreger	Resistente Erreger waren bislang selten
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	Keine klare Dosis-/Wirkungsbeziehung
	Variable Pharmakokinetik und -dynamik
Patienten	**Relativ seltene Erkrankung**
	Relativ hohe Letalität durch Grunderkrankung
	Diagnosekriterien waren lange Zeit uneinheitlich
	Wenige gesicherte Infektionen
	Infektionsdiagnose verzögert

Aspergillus to Zygomycetes: Causes, Risk Factors, Prevention, and Treatment of Invasive Fungal Infections

O. A. Cornely

Table 2
Mortality Rates for Specific Organism in IFIs.

Organism	Mortality (%)
Aspergillus species [43, 44]	
Overall case fatality rate	58
AIDS	86
HSCT	32–87
Leukemia/lymphoma	49
Blastomyces dermatitidis [3]	
Immunocompromised	30–49
Candida species [17, 45]	
Overall	10–49
Neutropenic	48

Infection 2008; 36: 296–313

Causes of Death in a Contemporary Cohort of Patients with Invasive Aspergillosis

Carolina Garcia-Vidal[1,2*], Maddalena Peghin[3],

152 Patienten mit Aspergillose:

Letalität 60 % (92/152)

***Aspergillus*-related N = 62**

***Aspergillus*-unrelated N = 36**

PLOS ONE | DOI:10.1371/journal.pone.0120370 March 24, 2015

In-vitro testing of susceptibility to amphotericin B is a reliable predictor of clinical outcome in invasive aspergillosis

C. Lass-Flörl[a*], G. Kofler[a], G. Kropshofer[c], J. Hermans[d], A. Kreczy[b], M. P. Dierich[a] and

Table II. MIC of amphotericin B against the isolated *Aspergillus* spp.

Species	*n*	MIC (mg/L)
A. terreus	9	⩾2
A. fumigatus	2	<2
	6	⩾2
A. flavus	4	<2
	8	⩾2

Table III. MIC of amphotericin B in relation to survival from disseminated fungal infections

	Outcome of disseminated infection		
MIC (mg/L)	dead	survivors	*P* value (Fisher's test)
<2	0	6	
⩾2	22	1	<0.001

Journal of Antimicrobial Chemotherapy (1998) **42**, 497–502

Azol-resistente *Aspergillus fumigatus* = ARAF

1945 – 1998: 170 *A. fumigatus*-Isolate

2002 – 2007: 10/81 resistent

Alle empfindlich

Itraconazol: > 16 mg/l

Voriconazol: 2 - > 16 mg/l

Posaconazol: 0.5 – 1 mg/l

cyp51A: TR_{34}/L98H und TR_{46}/Y121F/T289A

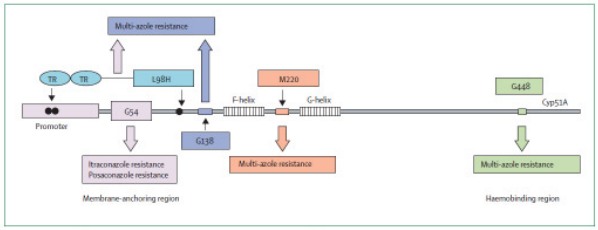


Figure 3: Aspergillus fumigatus cyp51A-related resistance mechanisms to azole antifungals
The position of the different mutations are shown with the associated phenotypes. MIC=minimum inhibitory concentration. TR=tandem repeat.

Verweij PE, Mellado E, Melchers WJG: Multiple triazole-resistent aspergillosis. NEJM 356 (2007): 1481-1483

Lancet Infect Dis 2009; 9: 789–95

Clinical Implications of Azole Resistance in *Aspergillus fumigatus*, the Netherlands, 2007–2009

Jan W.M. van der Linden, Eveline Snelders, Greetje A. Kampinga, Bart J.A. Rijnders, Eva Mattsson, Yvette J. Debets-Ossenkopp, Ed J. Kuijper, Frank H. Van Tiel, Willem J.G. Melchers, and Paul E. Verweij

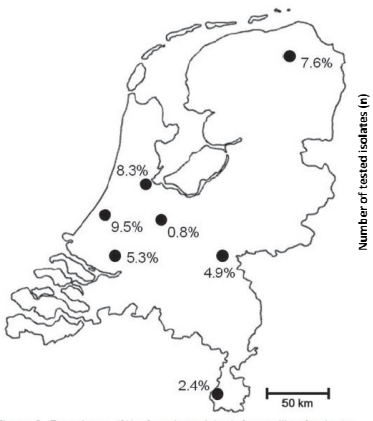
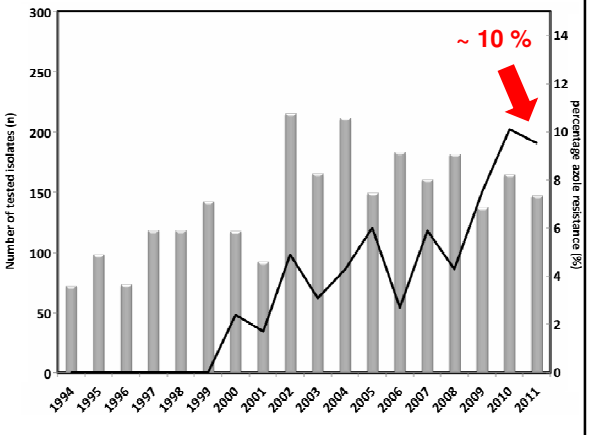


Figure 2. Prevalence (%) of azole-resistant *Aspergillus fumigatus* infections in university medical centers, the Netherlands, 2007–2009.



ICAAC 2014, M-319
D. Versteeg et al.: Continued increase of azole resistance in Aspergillus fumigatus (Af) in Dutch Hospitals

Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 17, No. 10, October 2011

Frequency and Evolution of Azole Resistance in *Aspergillus fumigatus* Associated with Treatment Failure[1]

Susan J. Howard, Dasa Cerar, Michael J. Anderson, Ahmed Albarrag, Matthew C. Fisher, Alessandro C. Pasqualotto, Michel Laverdiere, Maiken C. Arendrup, David S. Perlin, and David W. Denning

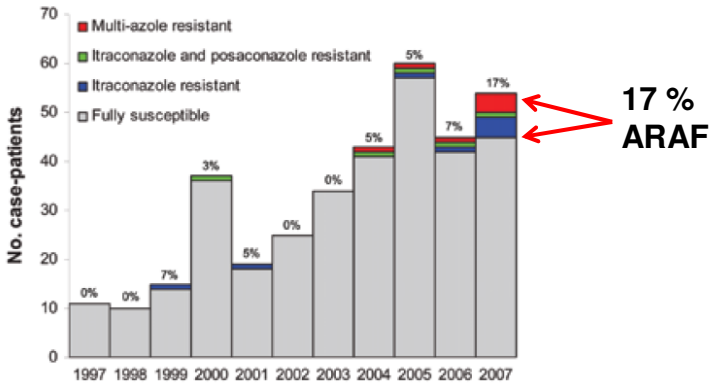


Figure 1. Azole resistance in clinical *Aspergillus fumigatus* isolates received in the Regional Mycology Laboratory Manchester, UK, 1997–2007. Overall azole resistance for each year is shown above each column as a percentage. Data do not include sequential isolates from the same patient.

Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 15, No. 7, July 2009

ARAF in Deutschland

Azole-resistant invasive aspergillosis in a patient with acute myeloid leukaemia in Germany

A Hamprecht (axel.hamprecht@uk-koeln.de)[1], D Buchheidt[2], J J Vehreschild[3], O A Cornely[3,4], B Spiess[2], G Plum[1], T V Halbsguth[3], N Kutsch[3], D Stippel[5], P Kahl[6], T Persigehl[7], A Steinbach[3], B Bos[3], M Hallek[3], M J Vehreschild[3]

Euro Surveill. 2012;17(36):pii=20262.

Antimicrobial Agents and Chemotherapy

First Reported Case of Azole-Resistant Aspergillus fumigatus Due to the TR/L98H Mutation in Germany

P.-M. Rath, D. Buchheidt, B. Spiess, E. Arfanis, J. Buer and J. Steinmann

Antimicrob. Agents Chemother. 2012, 56(11):6060. DOI:

Azol-Resistenz bei Aspergillus fumigatus – Epidemiologie und Nachweis bei immunsupprimierten Patienten in Deutschland

D. Buchheidt[1] B. Spiess[1] O.A. Cornely[2,3] M.J. G. T. Vehreschild[2] A. Hamprecht[4] P.-M. Rath[5] J. Steinmann[5] U. Groß[6] O. Bader[6] M. Lauten[7] M. Reinwald[1] W.-K. Hofmann[1]

Dtsch Med Wochenschr 2014; 139: 1373–1376 · © Georg

Environmental Isolates of Azole-Resistant *Aspergillus fumigatus* in Germany

Oliver Bader,[a] Jana Tünnermann,[a] Anna Dudakova,[a] Marut Tangwattanachuleeporn,[a,b] Michael Weig,[a] Uwe Groß,[a] MykoLabNet-D

12 % ARAF

TABLE 1 Drug resistance patterns

Cyp51A isoform	*n*	MIC_0 range (μg · ml^{-1}) Itraconazole	Voriconazole	Posaconazole
TR_{34}/L98H	45	>32	1 to 4 and >32[a]	0.125 to 0.5
TR_{46}/Y121F/T289A	5	1 to 2	4 to >32	1
TR_{46}/Y121F/M172I/T289A	1	1	>32	0.5
G54A	2	>32	0.125	1
M220I	1	>32	1	0.5
Wild type	1	>32	8	1

[a] Forty-four isolates with MIC_0 values within the range of 1 to 4, and one isolate at >32.

Antimicrobial Agents and Chemotherapy July 2015 Volume 59 Number 7

Emergence of azole-resistant invasive aspergillosis in HSCT recipients in Germany

J. Steinmann[1]*†, A. Hamprecht[2]†, M. J. G. T. Vehreschild[3,4], O. A. Cornely[3-5], D. Buchheidt[6], B. Spiess[6], M. Koldehoff[7], J. Buer[1], J. F. Meis[8,9] and P.-M. Rath[1]

762 Patienten mit HSCT. 27 Patienten (3.5%) *A. fumigatus*, ARAF bei 8 (~ 30%).

Patient no.	Sex, age (years)	Underlying disease	Type of mutation	MIC (mg/L) ITC	VRC	POS	Antifungal treatment	Discharge status (100 days after ARAF detection)	Cause of death
1	M, 46	AML	TR_{34}/L98H	>16	2	0.5	CAS	died	sepsis
2	M, 54	AML	WT	>16	4	0.5	VRC	died	relapse, MOV
3	F, 65	AML	TR_{34}/L98H	>16	4	0.5	POS	died	sepsis, MOV
4	M, 66	Acute biphenotype leukaemia	TR_{34}/L98H	>16	2	0.5	L-AMB, later VRC	died	sepsis, MOV
5	F, 58	MDS RAEB-II	TR_{34}/L98H	>16	2	0.5	VRC	died	sepsis, MOV
6	F, 38	Plasma cell leukaemia	TR_{34}/L98H	>16	2	0.5	VRC	alive	—
7	M, 43	CLL Binet C	TR_{46}/Y121F/ T289A	>16	16	0.5	L-AMB, later VRC	died	GvHD, MOV
8	F, 52	Follicular B-NHL grade IIIa	TR_{46}/Y121F/ T289A	1	>16	0.5	L-AMB, later CAS	died	sepsis

7/8 Patienten verstorben, aber nicht an der *Aspergillus*-Infektion (alleine).

J Antimicrob Chemother 2015; **70**: 1522–1526

Epidemiology of invasive aspergillosis and azole resistance in patients with acute leukaemia: the SEPIA Study

Philipp Koehler [a,b], Axel Hamprecht [c,d], Oliver Bader [e], Isabelle Bekeredjian-Ding [f], Dieter Buchheidt [g], Gottfried Doelken [h], Johannes Elias [i], Gerhard Haase [j], Corinna Hahn-Ast [f], Meinolf Karthaus [k], Alexander Kekulé [l], Peter Keller [m,1], Michael Kiehl [n], Stefan W. Krause [o], Carolin Krämer [j], Silke Neumann [c,2], Holger Rohde [p], Paul La Rosée [m], Markus Ruhnke [q], Philippe Schafhausen [r], Enrico Schalk [s], Katrin Schulz [h], Stefan Schwartz [q], Gerda Silling [t,3], Peter Staib [u], Andrew Ullmann [v], Maria Vergoulidou [q], Thomas Weber [l], Oliver A. Cornely [a,b,d,w], Maria J.G.T. Vehreschild [a,d,*]

2011 – 2013:

179 Aspergillose-Fälle (3.4% gesichert)

Inzidenz 6.4% bei AML (2440 Patienten)

3.8% bei ALL (627 Patienten)

ca. 30 % „complete response“

77 Isolate – 2 Fälle ARAF (TR_{34}/L98H) = 1.1 %

International Journal of Antimicrobial Agents 49 (2017) 218–223

Azole Resistance in *Aspergillus fumigatus*: Can We Retain the Clinical Use of Mold-Active Antifungal Azoles?

Paul E. Verweij,[1] Anuradha Chowdhary,[2] Willem J. G. Melchers,[1] and Jacques F. Meis[1,3]

Table 3. Reported Mortality Rates in Patients With Invasive Aspergillosis in Different T

		Aspergillus Disease
Era	IA	Comment
c-AmB era	65% [2]	122 of 187 patients receiving c-AmB died.
	71.6% [55]	187 of 261 patients with IA died.
Azole era	27.5% [57]	9-wk mortality: 39 of 142 patients receiving voriconazole monotherapy.
	28.5% [58]	Population-based study analyzing 8563 aspergillosis cases in France.
Azole resistant	100% [44]	Culture-positive patients with proven and probable IPA treated with voriconazole (5/5)
	88% [45]	8 HSCT patients with culture-positive, azole-resistant IA, of whom 7 died.
	100% [54]	ICU patients with culture-positive azole-resistant IA died (10/10), compared with 21 of 28 (75%) with azole-susceptible IA.

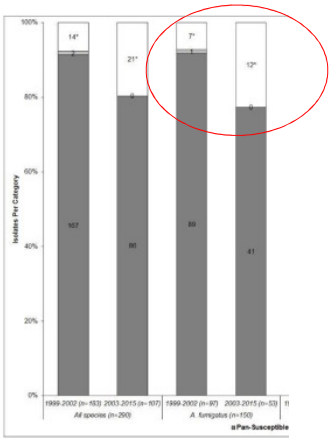
Clinical Infectious Diseases® 2016;62(3):362–8

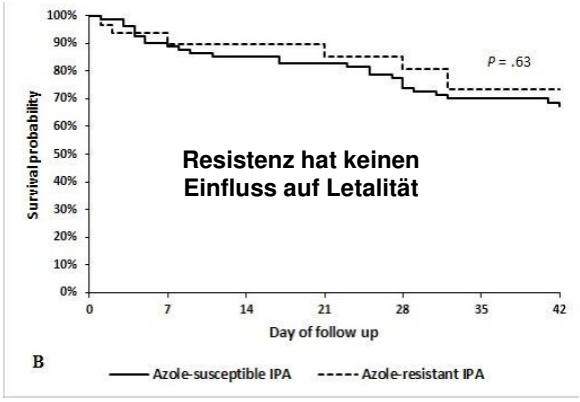
Changes in in vitro susceptibility patterns of *Aspergillus* to triazoles and correlation with aspergillosis outcome in a tertiary care cancer center (1999-2015)

Sang Taek Heo#,[1,2] Alexander M. Tatara#,[1,2] Cristina Jiménez-Ortigosa,[1] Ying Jiang,[1] Russell E Lewis,[1*] Jeffrey Tarrand,[2] Frank Tverdek,[3] Nathaniel D. Albert,[3] Paul E. Verweij,[4] Jacques F Meis,[4] Antonios G. Mikos,[5] David S. Perlin,[6] Dimitrios P. Kontoyiannis[1]

290 Isolate, 37 resistent (13%), kein Polymorphismus

MHK niedrig (Itraconazol < 8 mg/l, Voriconazol < 4 mg/l)





Azole in den letzten 3 Monaten OR 9.6

CID 31.3.17, doi.org/10.1093/cid/cix297

Herkunft von ARAF

Patient

- **Prolongierte Azol-Therapie**
- **Chronische pulmonale Aspergillose**
- **Mutationen im Cyp51A-Gen oder unbekannter Mechanismus**
- **Verschiedene Resistenzmechanismen in Isolaten eines Patienten**

Umgebung

- **Mehrzahl der Patienten ohne Azol-Anamnese**
- **Invasive Aspergillose oder chronische Infektion**
- **Wenige Resistenzmechanismen**

Lancet Infect Dis 2009; 9:789-95

Role of Antifungal Susceptibility Testing in Non-*Aspergillus* Invasive Mold Infections

Frédéric Lamoth,[a,b,c,d] Lauro Damonti,[c] Barbara D. Alexander[a,b]

TABLE 3 Response to amphotericin B therapy at week 6 for various MIC cutoffs

MIC cutoff (μg/ml)	Response rate (no. [%]) ($n = 10^a$)		
	MIC ≤ cutoff	MIC > cutoff	*P* value
0.25	2/2 (100)	3/8 (38)	0.40
0.5	5/6 (83)	0/4 (0)	0.05
1	5/7 (71)	0/3 (0)	0.17
2	5/7 (71)	0/3 (0)	0.17
4	5/8 (63)	0/2 (0)	0.44

[a] *Rhizopus* spp. ($n = 6$), *Mucor* spp. ($n = 1$), *Cunninghamella* spp. ($n = 1$), *Scedosporium apiospermum* ($n = 1$), *Purpureocillium lilacinum* ($n = 1$).

For amphotericin B, an MIC of ≤0.5 μg/ml was significantly associated with better 6-week outcomes.

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Zusammenfassung

Relevanz der Ergebnisse von Empfindlichkeitsbestimmungen

Candida	**Amphotericin B**	**?**
	Azole	**+++**
	Echinocandine	**++**
Aspergillus	**Amphotericin B**	**+**
	Azole	**+++**
	Echinocandine	**?**
Non-*Aspergillus*-Spezies	**Amphotericin B**	**(+)**

Welche Isolate testen?

Alle Isolate aus epidemiologischen Gründen: **fakultativ**

Nur invasive, exakt identifizierte Isolate:

Candida albicans	**Fluconazol**
Candida glabrata	**Fluconazol, Echinocandin**
***Aspergillus* spp.**	**Itraconazol**
Non-*Aspergillus*-Arten	**Amphotericin B ? (Referenzlabor)**

Nicht erst bei Therapieversagen !