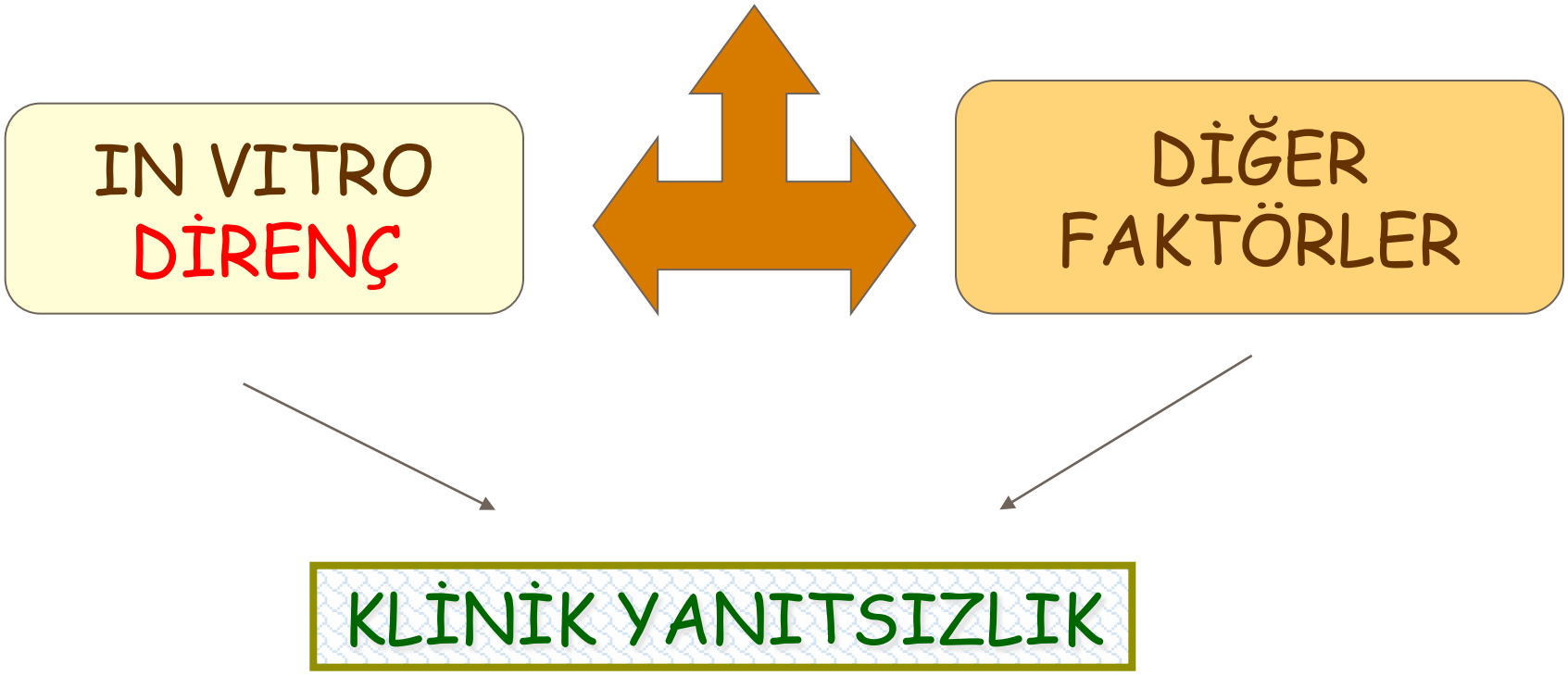
6. Türkiye EKMUD Kongresi 11-15 Mayıs 2016, Antalya KURS 3:
SİSTEMİK FUNGAL ENFEKSİYONLARDA
TANI ve TEDAVİ

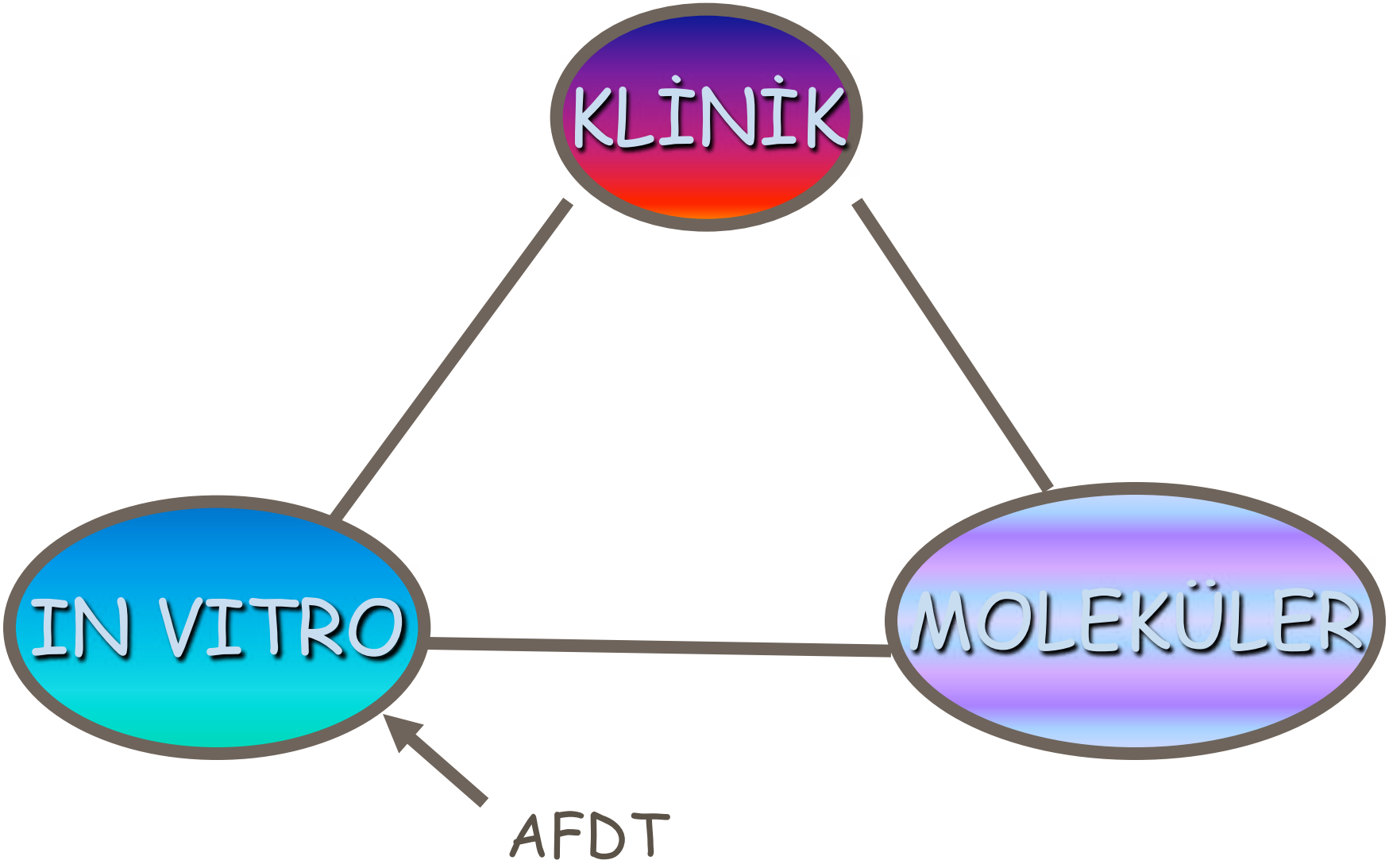
Antifungal Duyarlılık Testleri

Prof. Dr. Sevtap ARIKAN AKDAĞLI
Hacettepe Üniversitesi Tıp Fak. Tıbbi Mikrobiyoloji AD

İFE -Tedavi Başarısızlığı



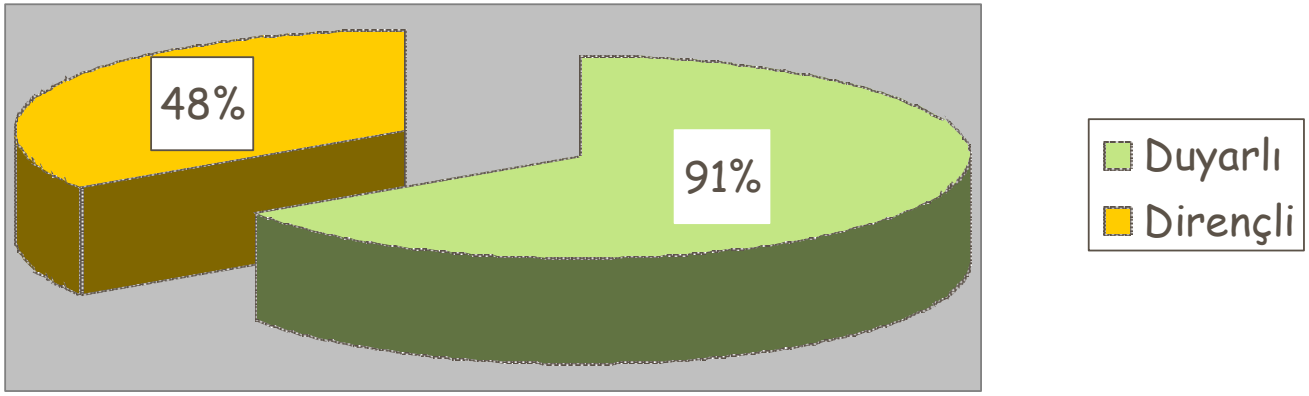
DİRENÇ



Antifungal duyarlılık testlerine gereksinim

- İmmünsupresif konak ↑
- Nadir türler
- Yeni bileşikler
- Direnç

AFDT - Klinik yanıt tahmini



Candida -flukonazol

Candida - itrakonazol

Candida - ketokonazol

C. neoformans - flukonazol

Histoplasma - flukonazol

Rex et al. CID 2002; 35: 982

AFDT, uygun tdv belirlenmesi için yararlı ama IFI mortalitesi *genelde* erken tedavi başlananlarda bile yüksek...

Timing of susceptibility-based antifungal drug administration in patients with *Candida* bloodstream infection: correlation with outcomes

Shellee A. Grim[1,2*], Karen Berger[1†], Christine Teng[3], Sandeep Gupta[4], Jennifer E. Layden[2], William M. Janda[5] and Nina M. Clark[2]

Ancak, ≥24 saat süre uygun antifungal tedavi alan hasta grubunda, pozitif kan kültürü sonucundan sonra 72 saat içinde uygun tdv. başlanmış hastalardaki mortalite, >72 saatte başlananlardan anlamlı ölçüde daha düşük (%27 - %40; p=0.004)

(*n*=231) (*n*=215)

Time to appropriate antifungal therapy

Figure 1. The 30 day mortality based on the time to initiation of appropriate antifungal therapy. *P*=0.11 between ≤72 and >72 h.

dictors of mortality. A secondary analysis requiring patients in the early treatment group to have received ≥24 h of effective antifungal therapy did show a significant mortality benefit to receiving antifungal treatment within 72 h of a positive blood culture being drawn (30 day mortality for early treatment: 27% versus 40%, *P*=0.004; HR for mortality with delayed treatment on multivariable analysis: 1.41, 95% CI 1.01–1.98, *P*=0.045).

- AFDT için Rutin Endikasyonlar ve Güncel Uygulama Önerileri

Candida-AFDT
ESCMID-Candida kılavuzu

ESCMID guideline for the diagnosis and management of Candida diseases: Diagnostic procedures. CMI 2012; 18 (Suppl. 7): 9

İzolasyon yeri	RUTİN Amaçlı Öneriler	EPİDEMİYOLOJİK Amaçlı Öneriler
Kan ve diğer steril bölgeler	•Tüm izolatlar, özellikle: 1.Antifungal ilaç kullanmış olan olgulardan izole edilen suşlar 2.Klinik yanıtsızlık 3.Nadir ve yeni ortaya çıkan türler 4.Klinik kullanımdaki antifungal ilaç(lar)a dirençli veya daha az duyarlı oldukları bilinen türler	Tüm izolatlar referans bir yöntem veya (geçerliliği kabul edilmiş ticari bir sistem) ile test edilmeli
Yüzeyel bölgeler	•Tedaviye yanıt vermeyen veya tekrarlayan enfeksiyon •Antifungal ilaç kullanmış hastalardan sürveyans kültürleri	Periyodik epidemiyolojik çalışmalar yapılmalı

Pfaller et al. Clin Microbiol Rev 2006; 19: 435; Reyes et al. Drug Resist Update 2000; 3: 14; Rex et al. CID 2002; 35: 982; Hospenthal et al. DMID 2004; 48: 153

Candida-AFDT için farklı kriterlere göre ayrıntılı görüş ve öneriler (CLSI) -I

TABLE 5 Recommendations for use of antifungal susceptibility testing of *Candida* spp. in the clinical laboratory

Clinical setting	Recommendation(s)
Routine	Species-level identification of all *Candida* isolates from deep sites (e.g., blood, normally sterile body fluids, tissues, abscesses) Routine antifungal testing of fluconazole and an echinocandin against *C. glabrata* from deep sites Routine testing of fluconazole and an echinocandin against other species of *Candida* possibly helpful but susceptibility usually predictable by species Use CBPs or ECVs to interpret results as appropriate (Table 1) Consider cross-resistance between fluconazole and all other azoles to be complete for *C. glabrata* Create an antifungogram
Mucosal candidiasis	Determination of azole susceptibility not routinely necessary Susceptibility testing of azoles may be useful for patients unresponsive to therapy
Invasive disease with clinical failure of initial therapy	Consider susceptibility testing as an adjunct—amphotericin B, flucytosine, fluconazole, voriconazole, and an echinocandin Consultation with an experienced microbiologist recommended
Infection with species with high rates of intrinsic or acquired resistance	Susceptibility testing not necessary when intrinsic resistance is known *C. lusitaniae* and amphotericin *C. krusei* and fluconazole, flucytosine *C. guilliermondii* and echinocandins With high rates of acquired resistance, monitor closely for signs of failure and perform susceptibility testing *C. glabrata* and fluconazole, amphotericin B, and echinocandins *C. krusei* and amphotericin B *C. guilliermondii* and amphotericin B *C. rugosa* and amphotericin B, fluconazole, and echinocandins

Pfaller and Diekema. J Clin Microbiol 2012; 50: 2846

Candida-AFDT için farklı kriterlere göre ayrıntılı görüş ve öneriler (CLSI) -II

New treatment options (e.g., echinocandins, voriconazole, posaconazole) or unusual species	Susceptibility of *Candida* spp. to echinocandins may be assumed unless initial response is suboptimal Susceptibility testing warranted if prior exposure to echinocandins or fluconazole Selection of therapy based on published consensus guidelines (52) and review of survey data on the organism-drug combination in question Susceptibility testing may be helpful when patient is not responding to what should be effective therapy
Patients who respond to therapy despite being infected with an organism later found to be resistant	Best approach not clear Take into account severity of infection, patient immune status, consequences of recurrent infection, etc. Consider alternative therapy for infections with isolates that appear to be highly resistant to initial therapy

Pfaller and Diekema. J Clin Microbiol 2012; 50: 2846

Candida-AFDT için ECIL-2011 önerileri

"Hematolojik hastalarda kan veya steril vücut bölgelerinden izole edilen suşlarda AFDT şu amaçlarla yapılmalıdır:"

-klinik yanıtsızlık veya mikrobiyolojik eradikasyonun sağlanamaması durumunda olası nedenin değerlendirilmesi	A II
- başlanan antifungal tedavide değişiklik kararının desteklenmesi	B II
-IV antifungal ilaçtan oral azole geçiş kararının desteklenmesi	A II

Küfler için AFDT: Rutin için öneriler

- CLSI M38-A2

- EUCAST E.Dis 9.3

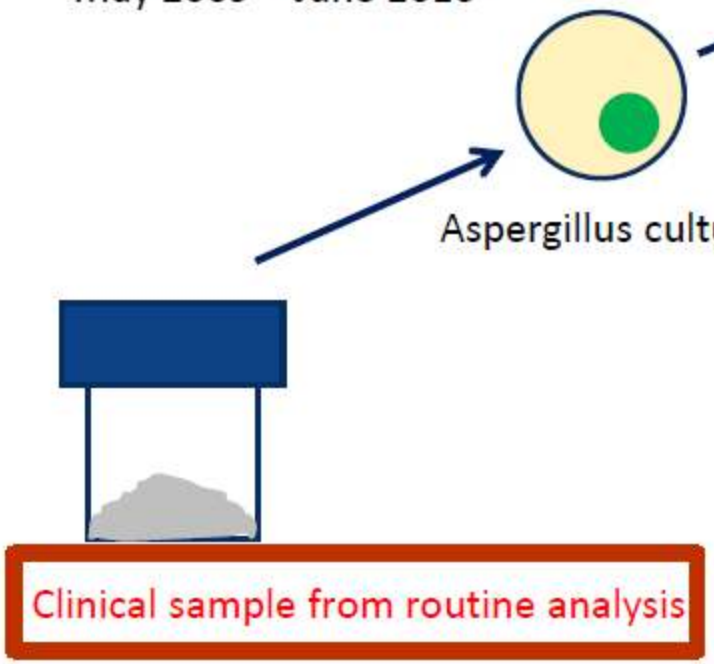
Aspergillus

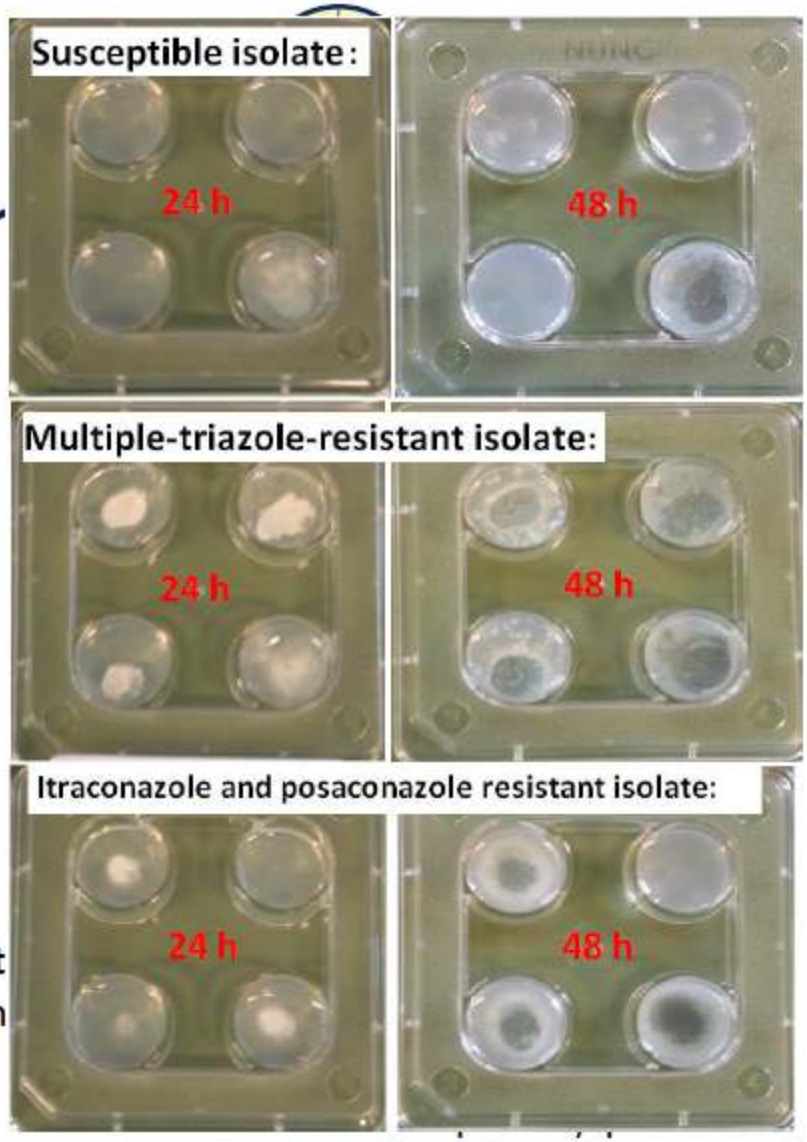
Aspergillus –Azole R; Agar Tarama Testi

UMC St Radboud

Surveillance-method

Prospective, multicenter surveillance
May 2009 – June 2010





• Complet
questionn

• Cyp-sequencing

www.umcn.nl

Courtesy of Paul Verweij & Jan van der Linden

Aspergillus – Azole direnci

Prospective Multicenter International Surveillance of Azole Resistance in *Aspergillus fumigatus*

J.W.M. van der Linden, M.C. Arendrup, A. Warris, K. Lagrou, H. Pelloux, P.M. Hauser, E. Chryssanthou, E. Mellado, S.E. Kidd, A.M. Tortorano, E. Dannaoui, P. Gaustad, J.W. Baddley, A. Uekötter, C. Lass-Flörl, N. Klimko, C.B. Moore, D.W. Denning, A.C. Pasqualotto, C. Kibbler, S. Arikan-Akdagli, D. Andes, J. Meletiadis, L. Naumiuk, M. Nucci, W.J.G. Melchers, P.E. Verweij

To investigate azole resistance in clinical *Aspergillus* isolates, we conducted prospective multicenter international surveillance. A total of 3,788 *Aspergillus* isolates were screened in 22 centers from 19 countries. Azole-resistant *A. fumigatus* was more frequently found (3.2% prevalence) than previously acknowledged, causing resistant invasive and noninvasive aspergillosis and severely compromising clinical use of azoles.

Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 21, No. 6, June 2015

International expert opinion on the management of infection caused by azole-resistant *Aspergillus fumigatus*

Drug Resistance Updates 21–22 (2015) 30–40

Paul E. Verweij[a,*], Michelle Ananda-Rajah[b], David Andes[c], Maiken C. Arendrup[d], Roger J. Brüggemann[e], Anuradha Chowdhary[f], Oliver A. Cornely[g], David W. Denning[h], Andreas H. Groll[i], Koichi Izumikawa[j], Bart Jan Kullberg[k], Katrien Lagrou[l], Johan Maertens[m], Jacques F. Meis[a,n], Pippa Newton[h], Iain Page[h], Seyedmojtaba Seyedmousavi[a], Donald C. Sheppard[o], Claudio Viscoli[p], Adilia Warris[q], J. Peter Donnelly[r]

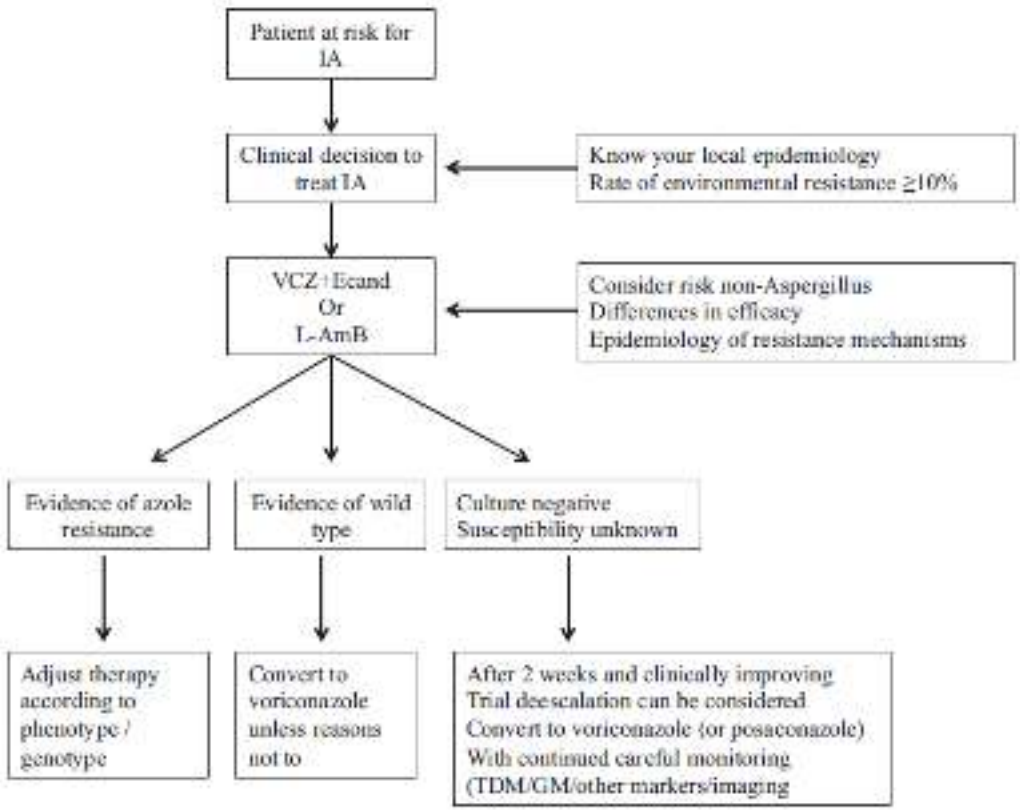


Fig. 3. Management of patients with clinical suspicion of IPA in regions with environmental resistance of ≥10%. IA, invasive aspergillosis; L-AmB, liposomal amphotericin B; VCZ, voriconazole; Ecand, echinocandin; TDM, therapeutic drug monitoring; GM, galactomannan.

Aspergillus- AFDT

Preliminary Results

Population	Intention	Intervention	SoR	QoE	References	Comment
All clinically relevant *Aspergillus* isolates (in patient groups or regions with known azole resistance)	Identify azole resistance	MIC test (always and routine)	A	II	Fraczek JAC 2013 Bueid JAC 2010 van der Linden CID 2013 Kuipers AAC 2011 Arendrup PLoS One 2010 van der Linden CID 2009 Badali Mycoses 2013 Chowdhary PLoS One 2012 Mortensen AAC 2010 Arendrup Drug Resist Updat 2014 Vermeulen Euro Surveill 2012 Camps AAC 2012 Stensvold Curr Fungal Infect Rep 2012 Chowdhary JAC 2012 Rath AAC 2012; SCARE study	As the initial and only test in situations where rapid testing is not available
		Routine agar screening only	B	III		.If MIC is not available .No validated assays - Refer to reference lab. for MIC testing if growth observed on screening agar

Mucorales - AFDT

ESCMID† and ECMM‡ joint clinical guidelines for the diagnosis and management of mucormycosis 2013

O. A. Cornely[1,†,‡,§], S. Arikan-Akdagli[2,‡,§], E. Dannaoui[3,§], A. H. Groll[4,†,‡,§], K. Lagrou[5,‡,§], A. Chakrabarti[6,§], F. Lanternier[7,8], L. Pagano[9], A. Skiada[10], M. Akova[2], M. C. Arendrup[11], T. Boekhout[12,13,14], A. Chowdhary[15], M. Cuenca-Estrella[16,†,‡], T. Freiberger[17,18,†], J. Guinea[19,†,‡], J. Guarro[20,‡], S. de Hoog[12,‡], W. Hope[21,†], E. Johnson[22,‡], S. Kathuria[15], M. Lackner[23,‡], C. Lass-Flörl[23,†,‡], O. Lortholary[7,†,‡], J. F. Meis[24,25,†,‡], J. Meletiadis[26,‡], P. Muñoz[19,†], M. Richardson[27,28,†,‡], E. Roilides[29,†,‡], A. M. Tortorano[30,‡], A. J. Ullmann[31,†,‡], A. van Diepeningen[12], P. Verweij[25,32,†,‡] and G. Petrikkos[33,†,‡,§]

TABLE 5. Recommendations on susceptibility testing in mucormycosis

Population	Intention	Method/Finding	SoR	QoE	Comment	References
Any	To guide treatment	EUCAST/CLSI reference microdilution methods	C	IIu	Clinical relevance uncertain. No data available to correlate MIC and outcome	79,80,83
Any	To guide treatment	Correlation of MIC with *in vivo* outcome	C	IIu	For *Apophysomyces elegans*, limited retrospective data suggest correlation	83
Any	To guide treatment	Correlation of MIC/MFC with *in vivo* outcome	B	III	Animal, posaconazole better in *Rhizopus microsporus* and *Rhizopus oryzae* strains MIC 0.25 μg/mL than in those with MICs 2 μg/mL	82,84,85
Any	To establish epidemiological knowledge	Susceptibility testing	A	IIu	$n = 37$ $n = 36$ $n = 217$ $n = 45$ $n = 77$ $n = 18$, *Apophysomyces elegans* $n = 21$ $n = 66$ Review	86 88 87 21 92 83 91 90 195
Any	To establish epidemiological knowledge	MIC determined by reference method	A	III	e.g. Etest® not validated for Mucorales	79,80

MFC, minimum fungicidal concentration; QoE, quality of evidence; SoR, strength of recommendation.

Fusarium ve Scedosporium - AFDT

ESCMID and ECMM joint guidelines on diagnosis and management of hyalohyphomycosis: *Fusarium* spp., *Scedosporium* spp. and others

A. M. Tortorano[1,*,†], M. Richardson[2,3,*,†,‡], E. Roilides[4,*,†,‡], A. van Diepeningen[5,*], M. Caira[6,*], P. Munoz[7,*,‡], E. Johnson[8,*,†], J. Meletiadis[9,*,†], Z.-D. Pana[4,*], M. Lackner[10,*,†], P. Verweij[11,12,*,†,‡], T. Freiberger[13,*,‡], O. A. Cornely[14,†,‡], S. Arikan-Akdagli[15,†], E. Dannaoui[16,†], A. H. Groll[17,†,‡], K. Lagrou[18,†], A. Chakrabarti[19], F. Lanternier[20,21], L. Pagano[22,†], A. Skiada[23,‡], M. Akova[15,‡], M. C. Arendrup[24,†,‡], T. Boekhout[5,25,26,†], A. Chowdhary[27,‡], M. Cuenca-Estrella[28,†,‡], J. Guinea[7,†,‡], J. Guarro[29,†], S. de Hoog[5,†], W. Hope[30,‡], S. Kathuria[27], O. Lortholary[31,32,†,‡], J. F. Meis[11,33,†,‡], A. J. Ullmann[34,†,‡], G. Petrikkos[35,*,†,‡] and C. Lass-Flörl[10,*,†,‡]

TABLE 4. Summary of recommendations for diagnosis of *Fusarium* infection

Fusarium infection/ Population	Test	SoR	QoE	Comment	References
	Susceptibility testing	C	III	Gives an overview of drug activity and may be helpful in selecting antifungals	[2,181,182,193–195]

TABLE 7. Summary of recommendations for diagnosis of *Scedosporium* infections

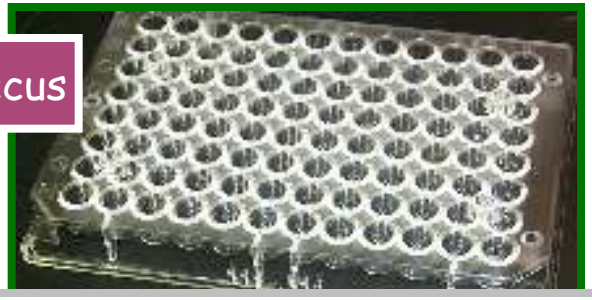
Population	Test	SoR	QoE	Comment	References
	In vitro susceptibility testing	C	III	Gives an overview of drug activity and therefore may support choice of antifungals	[221–223]

Clin Microbiol Infect 2014; **20** (Suppl. 3): 27–46

- Referans AFDT Yöntemleri

Referans Antifungal Duyarlılık Testi Yöntemleri -I

CLSI M27-A3 — Candida, Cryptococcus



CLSI M38-A2 — Aspergillus, Rhizopus, Fusarium, P. boydii, S. schenckii-küf formu , **dermatofitler**, dematisiyöz küfler

CLSI M44-A2 — Candida

CLSI M51-A — Dermatofit dışı küfler

CLSI-Ek Dökümanlar

M27-S4

M27-A3 için güncellenmiş tablolar 28/12/2012

M44-S3

M44-A2 yöntemi için KK değerleri 28/08/2009

M51-S1

M51-A yöntemi için KK ve ECV değerleri 05/2010

Referans Antifungal Duyarlılık Testi Yöntemleri -II

EUCAST E.Dis 7.3

Candida, Cryptococcus

EUCAST DEFINITIVE DOCUMENT E.DEF 7.3

Method for the determination of broth dilution minimum Inhibitory concentrations of antifungal agents for yeasts

December 2015

M. C. Arendrup[1], J Guinea[2], M. Cuenca-Estrella[3], J. Meletiadis[4,5], J. W. Mouton[5,6], K. Lagrou[7], S. J. Howard[8] and the Subcommittee on Antifungal Susceptibility Testing (AFST) of the ESCMID European Committee for Antimicrobial Susceptibility Testing (EUCAST)*

*EUCAST-AFST: MC Arendrup[1] (Chairman, Denmark), S Arikan-Akdagli[9] (Turkey), F Barchiesi[10] (Italy), M Castanheira[11] (USA), E Chryssanthou[12] (Sweden), J Guinea[2] (Steering Committee, Spain), P Hamal[13] (Czech Republic), SJ Howard[8] (Scientific Secretary, UK), H Järv[14] (Estonia), N Klimko[15] (Russia), P Koukila-Kähkölä[16] (Finland), O Kurzai[17] (Germany), K. Lagrou[7] (Steering Committee, Belgium), C Lass-Flörl[18] (Austria), M Mares[19] (Romania), T Matos[20] (Slovenia), J Meletiadis[4,5] (Scientific Data Coordinator, Greece), C Moore[21] (UK), JW Mouton[5,6] (EUCAST Steering Committee representative), K Muehlethaler[22] (Switzerland), T Rogers[23] (Ireland).

EUCAST E.Dis 9.3

Konidyum oluşturan küfler

EUCAST DEFINITIVE DOCUMENT E.DEF 9.3

Method for the determination of broth dilution minimum inhibitory concentrations of antifungal agents for conidia forming moulds

December 2015

M. C. Arendrup[1], J Guinea[2], M. Cuenca-Estrella[3], J. Meletiadis[4,5], J. W. Mouton[5,6], K. Lagrou[7], S. J. Howard[8] and the Subcommittee on Antifungal Susceptibility Testing (AFST) of the ESCMID European Committee for Antimicrobial Susceptibility Testing (EUCAST)*

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Alman referans yöntemi, DIN-58940-84

EUCAST- Diğer Dökümanlar

"Rationale documents for antifungal agents"

Amphotericin B vs. Candida v 1.0
Amphotericin B vs. Aspergillus v 1.0
Anidulafungin vs. Candida v 2.0
Fluconazole vs. Candida v 2.0
Isavuconazole vs. Aspergillus v 1.0
Itraconazole vs. Candida v 1.0
Itraconazole vs. Aspergillus v 1.1
Micafungin vs. Candida v 1.0
Posaconazole vs. Candida v 1.0
Posaconazole vs. Aspergillus v 1.0
Voriconazole vs. Candida v 2.0
Voriconazole vs. Aspergillus v 1.0

www.eucast.org/antifungal_susceptibility_testing_afst/rationale_documents_for_antifungals/

CLSI M27-A3 ve EUCAST E.Dis 7.3 mikrodilüsyon test parametreleri

	CLSI M27-A3	EUCAST E.Dis 7.3
Besiyeri	RPMI-1640 (L-glutaminli, bikarbonatsız, glu: %0.2	RPMI-1640 (L-glutaminli, bikarbonatsız, glu: % 2)
İnokulum yoğunluğu	0.5-2.5 x 10^3 cfu / ml	1-5 x 10^5 cfu / ml
Mikrodilüsyon plakları	96 U-tabanlı	96 düz tabanlı
MİK okuma zamanı	24-72 sa	24-48 sa
MİK okuma yöntemi	Görsel	Spektrofotometrik (530 nm)



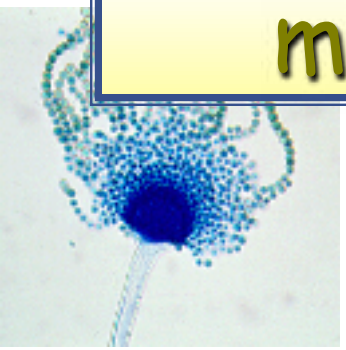

İnkübasyon süreleri, türe, ilaca, üreme yeterliliğine göre değişir.

M27-A3 MİK okuma zamanı ile ilgili ek ve ayrıntılı öneriler

Antifungal İlaç	MİK OKUMA ZAMANI (Yeterli üreme olduğunda!)	
	24 saat	48 saat
Amfoterisin B	EVET	EVET
Ekinokandinler	EVET	HAYIR
Flukonazol	EVET	EVET
Flusitozin	HAYIR	EVET
Itrakonazol	HAYIR	EVET
Posakonazol	HAYIR	EVET
Ravukonazol	HAYIR	EVET
Vorikonazol	HAYIR	EVET

Ref.: CLSI M27-A3

CLSI M38-A2 ve EUCAST E.Dis 9.3 mikrodilüsyon test parametreleri



	CLSI M38-A2	EUCAST E.Dis 9.3
Besiyeri	RPMI-1640 (L-glutaminli, bikarbonatsız, glu: %0.2	RPMI-1640 (L-glutaminli, bikarbonatsız, glu: % 2)
Inokulum yoğunluğu	Dermatofit dışı küfler: 0.4-5 x 10^4 cfu/ml Dermatofitler: 1-3x10^3cfu / ml	1-2.5 x 10^5 cfu / ml
Mikrodilüsyon plakları	96 U-tabanlı	96 düz tabanlı
MİK okuma zamanı	24-72sa (cinse ve üreme yeterliliğine göre değişir)	24-72sa (cinse ve üreme yeterliliğine göre değişir)
MİK okuma yöntemi	Görsel	Görsel

Önerilen MİK "okuma değerleri" ("MIC endpoint")

Amfoterisin B:	MİK-0
Flukonazol:	MİK-2 (Candida)
Itra, Posa, Vori:	MİK-0 (Aspergillus)
	MİK-1 (dermatofitler)
	MİK-2 (Candida)
Ekinokandinler:	MİK-2 (Candida)
	MEK (Aspergillus)
Siklopiroks:	MİK-1 (dermatofitler)
Grizeofulvin:	MİK-1 (dermatofitler)
Terbinafin:	MİK-1 (dermatofitler)

Wild-type MIC distributions, epidemiological cutoff values and species-specific clinical breakpoints for fluconazole and *Candida*: Time for harmonization of CLSI and EUCAST broth microdilution methods

M.A. Pfaller[a,*], D. Andes[b], D.J. Diekema[a], A. Espinel-Ingroff[c], D. Sheehan[d], The CLSI Subcommittee for Antifungal Susceptibility Testing

Drug Resistance Updates 13 (2010) 180–195

- Kl. direnç sınır değerleri
- ECV/ECOFF

Klinik Direnç Sınır Değerleri
ECV / ECOFF

Türe Özgü

Yönteme Özgü

İnkübasyon Süresine Özgü

C. glabrata-flukonazol: güncel duyarlılık kategorileri

C. glabrata,

Flukonazol MİK ≤ 32
=S-DD

Ref.: CLSI M27-A3

CLSI-Candida

Kl. direnç sınır değerleri ve/veya ECV

CLSI M27-S4 2012

Progress in Antifungal Susceptibility Testing of *Candida* spp. by Use of Clinical and Laboratory Standards Institute Broth Microdilution Methods, 2010 to 2012

M. A. Pfaller[a,b] and D. J. Diekema[b]

JMI Laboratories, North Liberty, Iowa, USA,[a] University of Iowa Carver College of Medicine, Iowa City, Iowa, USA[b]

Journal of Clinical Microbiology p. 2846–2856 September 2012 Volume 50 Number 9

EUCAST Direnç Sınır Değerleri; EUCAST web sitesi

EUCAST-Candida

***Candida* spp.**

EUCAST Antifungal Clinical Breakpoint Table v. 8.0 valid from 2015-11-16

MIC method (EUCAST standardised broth microdilution method)
Medium: RPMI 1640-2% glucose, MOPS buffer
Inoculum: Final $0.5 \times 10^5 - 2.5 \times 10^5$ cfu/mL
Incubation: 18-24h
Reading: Spectrophotometric; complete (>90%) inhibition for amphotericin B but 50% growth inhibition for other compounds
Quality control: *C. parapsilosis* ATCC 22019 or *C. krusei* ATCC 6258

Antifungal agent	MIC breakpoint (mg/L)														Notes
	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	1. Non-species related breakpoints have been determined mainly on the basis of PK/PD data and are independent of MIC distributions of specific species. They are for use only for organisms that do not have specific breakpoints.
Anidulafungin	0.03	0.03	0.06	0.06	0.06	0.06	0.002	4	0.06	0.06	IE[2]	IE[2]	IE	IE	2. The ECOFFs for these species are in general higher than for *C. albicans*.
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	3. Isolates that are susceptible to anidulafungin as well as micafungin should be considered susceptible to caspofungin, until caspofungin breakpoints have been established. Similarly, *C. parapsilosis* isolates intermediate to anidulafungin and micafungin can be regarded intermediate to caspofungin. EUCAST breakpoints have not yet been established for caspofungin, due to significant inter-laboratory variation in MIC ranges for caspofungin.
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	4. MICs for *C. tropicalis* are 1-2 two-fold dilution steps higher than for *C. albicans* and *C. glabrata*. In the clinical study successful outcome was numerically slightly lower for *C. tropicalis* than for *C. albicans* at both dosages (100 and 150 mg daily). However, the difference was not significant and whether it translates into a relevant clinical difference is unknown. MICs for *C. krusei* are approximately three two-fold dilution steps higher than those for *C. albicans* and, similarly, those for *C. guilliermondii* are approximately eight two-fold dilutions higher. In addition, only a small number of cases involved these species in the clinical trials. This means there is insufficient evidence to indicate whether the wild-type population of these pathogens can be considered susceptible to micafungin.
Itraconazole	0.06	0.06	IE[2]	IE[2]	IE[2]	IE[2]	0.12	0.12	0.12	0.12	IE[2]	IE[2]	IE	IE	
Micafungin	0.016	0.016	0.03	0.03	IE[4]	IE[4]	0.002	2	IE[4]	IE[4]	IE[4]	IE[4]	IE	IE	
Posaconazole	0.06	0.06	IE[2]	IE[2]	IE[2]	IE[2]	0.06	0.06	0.06	0.06	IE[2]	IE[2]	IE	IE	5. Strains with MIC values above the S/I breakpoint are rare or not yet reported. The identification and antifungal susceptibility tests on any such isolate must be repeated and if the result is confirmed the isolate sent to a reference laboratory. Until there is evidence regarding clinical response for confirmed isolates with MIC above the current resistant breakpoint they should be reported resistant.
Voriconazole	0.12[5]	0.12[5]	IE	IE	IE	IE	0.12[5]	0.12[5]	0.12[5]	0.12[5]	IE[2]	IE[2]	IE	IE	

Antimicrobial Agents and Chemotherapy p. 5836–5842

December 2013 Volume 57 Number 12

Interlaboratory variability of caspofungin MICs for *Candida* spp. using CLSI and EUCAST methods: Should the clinical laboratory be testing this agent?

A. Espinel-Ingroff[1*], M.C. Arendrup[2], M.A. Pfaller[3], L.X. Bonfietti[4], B. Bustamante[5], E. Canton[6], E. Chryssanthou[7], M. Cuenca-Estrella[8], E. Dannaoui[9], A. Fothergill[10], J. Fuller[11], P. Gaustad[12], G. M. Gonzalez[13], J. Guarro[14], C. Lass-Flörl[15], S.R. Lockhart[16], J.F. Meis[17], C.B. Moore[18], L. Ostrosky-Zeichner[19], T. Pelaez[20], S.R.B.S. Pukinskas[21], G. St-Germain[22], M.W. Szeszs[23], and J. Turnidge[24]

Although many factors (caspofungin powder source, stock solution solvent, powder storage time length and temperature, and MIC determination testing parameters) were examined as a potential cause of such unprecedented variability, a single specific cause was not identified. Therefore, it seems highly likely that the use of the CLSI species-specific caspofungin CBPs could lead to reporting an excessive number of wild-type [WT] (e.g., *C. glabrata* and *C. krusei*) as either non-WT or resistant isolates. Until this problem is resolved, routine testing or reporting of CLSI caspofungin MICs for *Candida* is not recommended; micafungin or anidulafungin data could be used instead.

CLSI-Asp

AND CHEMOTHERAPY, Nov. 2011, p. 5150–5154 Vol. 55, No. 11

Wild-Type MIC Distributions and Epidemiological Cutoff Values for Amphotericin B and *Aspergillus* spp. for the CLSI Broth Microdilution Method (M38-A2 Document)[▽]

A. Espinel-Ingroff,[1]* M. Cuenca-Estrella,[2] A. Fothergill,[3] J. Fuller,[4] M. Ghannoum,[5] E. Johnson,[6] T. Pelaez,[7] M. A. Pfaller,[8] and J. Turnidge[9]

CLSI& EUCAST combined data

TABLE 3. ECVs for amphotericin B and six *Aspergillus* spp., obtained using CLSI M38-A2 and/EUCAST broth microdilution methods at 48 h

Species	No. of isolates tested by CLSI/EUCAST method[a]	MIC (μg/ml):		Calculated statistical ECV (μg/ml)[d]		
		Range[b]	Mode[c]	≥95%	≥97.5%	≥99%
A. fumigatus	3,988/833	0.032–16	0.5/0.25/0.5	2/0.5/2[e]	2/1/2	4/1/4
A. flavus	793/194	0.032–8	1/1/1	2/2/2	4/2/4	4/2/4
A. nidulans	184/69	0.06–32	1/1/1	4/2/4	4/4/4	4/4/8
A. niger	673/140	0.03–2	0.5/0.25/0.5	2/0.5/2[e]	2/0.5/2	4/0.5/4
A. terreus	545/266	0.12–32	2/1/2	4/4/4	4/4/4	8/4/8
A. versicolor	135/22	0.032–8	1/1/1	2/2/2	2/4/2	2/4/4

[a] CLSI aggregated data from eight laboratories and EUCAST data from a single laboratory.
[b] Combined CLSI and EUCAST data.
[c] MIC most frequently obtained using CLSI/EUCAST/combined CLSI and EUCAST data.
[d] Calculated ECVs comprising ≥95, ≥97.5, or ≥99% of the statistically modeled population, obtained using CLSI/EUCAST/combined CLSI and EUCAST data.
[e] The ECV defined using the "eyeball" method, which included at least 95% of the observed (rather than the modeled) overall distribution, was 1 μg/ml.

CLSI

EUCAST

AMB-Asp

EUCAST, CLSI

CLSI-Asp

Azoller-Asp

CLSI

Wild-Type MIC Distributions and Epidemiological Cutoff Values for the Triazoles and Six *Aspergillus* spp. for the CLSI Broth Microdilution Method (M38-A2 Document)[▽]

A. Espinel-Ingroff,[1]* D. J. Diekema,[2] A. Fothergill,[3] E. Johnson,[4] T. Pelaez,[5] M. A. Pfaller,[2] M. G. Rinaldi,[3] E. Canton,[6] and J. Turnidge[7]

JOURNAL OF CLINICAL MICROBIOLOGY, Sept. 2010, p. 3251–3257 Vol. 48, No. 9

CLSI-Asp

İzavukonazol-Asp

CLSI

Multicenter Study of Isavuconazole MIC Distributions and Epidemiological Cutoff Values for *Aspergillus* spp. for the CLSI M38-A2 Broth Microdilution Method

A. Espinel-Ingroff,[a] A. Chowdhary,[b] G. M. Gonzalez,[c] C. Lass-Flörl,[d] E. Martin-Mazuelos,[e] J. Meis,[f,g] T. Peláez,[h] M. A. Pfaller,[i] J. Turnidge[j]

August 2013 Volume 57 Number 8 Antimicrobial Agents and Chemotherapy p. 3823–3828

EUCAST-Asp

Aspergillus spp.

EUCAST Antifungal Clinical Breakpoint Table v. 8.0 valid from 2015-11-16

MIC method (EUCAST standardised broth microdilution method)
Medium: RPMI1640 2% glucose, MOPS as buffer
Inoculum: Final 1x10(5) – 2.5x10(5) cfu/mL
Incubation: 48h
Reading: Visual, complete inhibition for amphotericin B and azoles (MIC), aberrant growth endpoint for echinocandins (MEC).
Quality control: *A. fumigatus* ATCC 204305, *A. flavus* ATCC 204304, *A. fumigatus* F 8910, *A. flavus* CM 1813, *C. parapsilosis* ATCC 22019 (read after 18-24 h) or *C. krusei* ATCC 6258 (read after 18-24 h)

Antifungal agent	MIC breakpoint (mg/L)												Notes
	A. flavus		*A. fumigatus*		*A. nidulans*		*A. niger*		*A. terreus*		Non-species related breakpoints[1]		
	S ≤	R >	S ≤	R >	S ≤	R >	S ≤	R >	S ≤	R >	S ≤	R >	
Amphotericin B	IE[2]	IE[2]	1	2	Note[4]	Note[4]	1	2	-	-	IE	IE	1. Non species related breakpoints have been determined mainly on the basis of PK/PD data and are independent of MIC distributions of specific species. They are for use only for organisms that do not have specific breakpoints.
Anidulafungin	IE	IE	IE	IE	IE	IE	IE	IE	IE	IE	IE	IE	2. The ECOFFs for these species are in general one step higher than for *A. fumigatus*
Caspofungin	IE	IE	IE	IE	IE	IE	IE	IE	IE	IE	IE	IE	3. There are too few MIC data to establish ECOFFs and hence to suggest any breakpoints.
Fluconazole	-	-	-	-	-	-	-	-	-	-	-	-	4. Monitoring of azole trough concentrations in patients treated for fungal infection is recommended.
Isavuconazole	IE[3]	IE[3]	1	1	0.25	0.25	IE[3]	IE[3]	1	1	IE	IE	5. The MIC values for isolates of *A. niger* and *A. versicolor* are in general higher than those for *A. fumigatus*. Whether this translates into a poorer clinical response is unknown.
Itraconazole[4]	1	2	1	2	1	2	IE[3,4]	IE[3,4]	1	2	IE[4]	IE[4]	6. Provided adequate drug exposure has been confirmed using therapeutic drug monitoring (TDM). There remains some uncertainty regarding cut-off values for posaconazole concentrations that separate patients with a high probability of clinical success from those with a low probability of clinical success. In some circumstances (e.g. patients with persistent and profound neutropenia, large lesions, or those with other features associated with a poor clinical outcome) a relatively high trough concentration should be sought. Preclinical and clinical data suggest this value should be >1 mg/L at steady state. For other patient groups a lower trough concentration may be acceptable. For prophylaxis a target concentration of >0.7 mg/L has been suggested.
Micafungin	IE	IE	IE	IE	IE	IE	IE	IE	IE	IE	IE	IE	
Posaconazole[4]	IE[3]	IE[3]	0.12[4]	0.25[4]	IE[3]	IE[3]	IE[3]	IE[3]	0.12[4]	0.25[4]	IE	IE	
Voriconazole[4]	IE[4]	IE[4]	1	2	IE	IE	IE[4]	IE[4]	IE[4]	IE[4]	IE	IE	

CLSI-Mucorales

Multicenter Evaluation of MIC Distributions for Epidemiologic Cutoff Value Definition To Detect Amphotericin B, Posaconazole, and Itraconazole Resistance among the Most Clinically Relevant Species of *Mucorales*

CLSI M38-A2

A. Espinel-Ingroff,[a] A. Chakrabarti,[b] A. Chowdhary,[c] S. Cordoba,[d] E. Dannaoui,[e] P. Dufresne,[f] A. Fothergill,[g] M. Ghannoum,[h] G. M. Gonzalez,[i] J. Guarro,[j] S. Kidd,[k] C. Lass-Flörl,[l] J. F. Meis,[m] T. Pelaez,[n] A. M. Tortorano,[o] J. Turnidge[p]

Antimicrobial Agents and Chemotherapy March 2015 Volume 59 Number 3

CLSI-Fusarium

International Evaluation of MIC Distributions and Epidemiological Cutoff Value (ECV) Definitions for *Fusarium* Species Identified by Molecular Methods for the CLSI Broth Microdilution Method

A. Espinel-Ingroff,[a] A. L. Colombo,[b] S. Cordoba,[c] P. J. Dufresne,[d] J. Fuller,[e] M. Ghannoum,[f] G. M. Gonzalez,[g] J. Guarro,[h] S. E. Kidd,[i] J. F. Meis,[j] T. M. S. C. Melhem,[k] T. Pelaez,[l] M. A. Pfaller,[m] M. W. Szeszs,[n] J. P. Takahaschi,[o] A. M. Tortorano,[p] N. P. Wiederhold,[q] J. Turnidge[r]

Antimicrob Agents Chemother 2015 Dec 7;60:1079-84

Yeni direnç sınır değerlerinin pratikte kullanımı -I

JCM 2013; 51: 2571

Michael A. Pfaller, Shawn A. Messer, Leah N. Woosley, Ronald N. Jones, Mariana Castanheira

JMI Laboratories, North Liberty, Iowa, USA

Echinocandin and Triazole Antifungal Susceptibility Profiles for Clinical Opportunistic Yeast and Mold Isolates Collected from 2010 to 2011: Application of New CLSI Clinical Breakpoints and Epidemiological Cutoff Values for Characterization of Geographic and Temporal Trends of Antifungal Resistance

SENTRY Antimicrobial Surveillance Program

34 ülkeden 98 merkezden
toplam 3418 mantar suşu
(2010-2011 yılları)

GENEL SONUÇ ve UYARI: Düşük oranda triazol ve ekinokandin direnci. C. glabrata suşlarında flukonazol ve ekinokandin direnci yönünden yakın izlem gerekli.

Yeni direnç sınır değerlerinin pratikte kullanımı -II

(Sensititre Yeast One)

Candida species distribution and antifungal susceptibility testing according to European Committee on Antimicrobial Susceptibility Testing and new vs. old Clinical and Laboratory Standards Institute clinical breakpoints: a 6-year prospective candidaemia survey from the fungal infection network of Switzerland

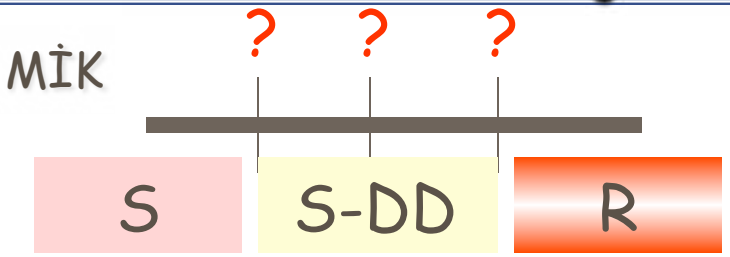
C. Orasch[1], O. Marchetti[1], J. Garbino[2], J. Schrenzel[3], S. Zimmerli[4], K. Mühlethaler[4], G. Pfyffer[5], C. Ruef[6], J. Fehr[6], R. Zbinden[7], T. Calandra[1], J. Bille[8] and the Fungal Infection Network of Switzerland (FUNGINOS)*

(*C. albicans*, *C. glabrata*, *C. tropicalis* and *C. parapsilosis*) represented >90% of all CBIs. *In vitro* resistance to fluconazole, voriconazole and caspofungin was rare among *C. albicans*, but an increase of non-susceptibile isolates was observed among *C. tropicalis*/*C. parapsilosis* for the azoles and *C. glabrata*/*C. krusei* for caspofungin according to EUCAST and new CLSI breakpoints compared with old CLSI breakpoints.

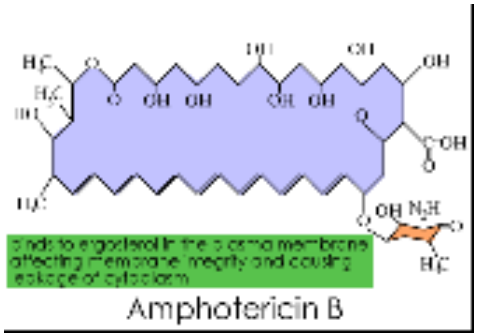
Yeni CLSI ve EUCAST direnç sınır değerleri ile, eski CLSI direnç sınır değerleri ile olana kıyasla, azollere dirençli C. tropicalis/ C.parapsilosis ve kaspofungine dirençli C. glabrata/ C. krusei suşlarında artış

Mikrodilüsyon referans AFDT'nin dezavantajları

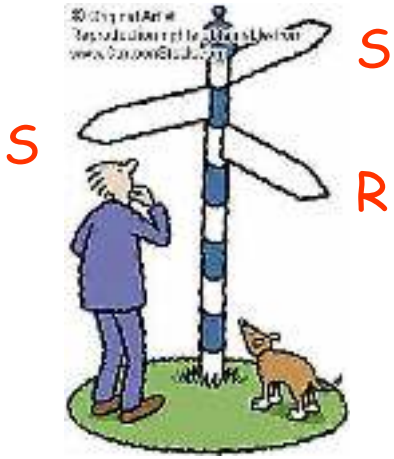
Sonuç: 24-72 saatte Başlangıç antifungal tedavisine sınırlı katkı



Klinik MİK direnç sınır değerleri tüm ilaç ve türler için henüz belirlenmiş değil. ("ECOFF" lar …)



In vitro amfoterisin B direnci?



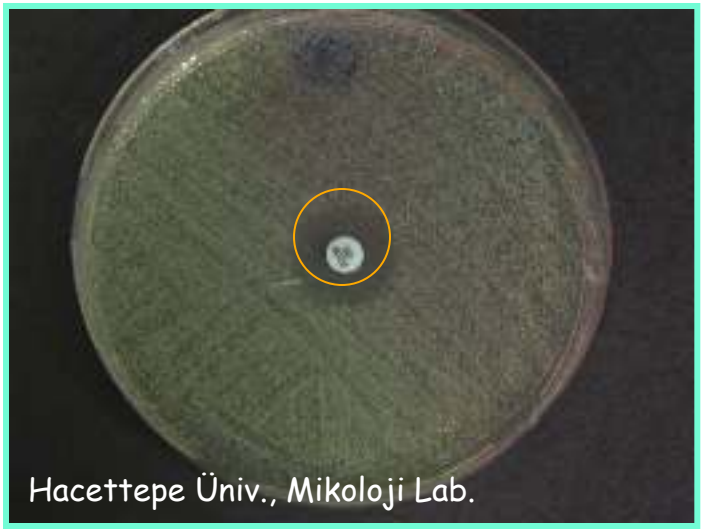
"Heavy trailer" Candida-azoller

- Disk difüzyon

Disk difüzyon-Candida

CLSI, M44-A2

RPMI- % 2 glu, Flu, 24sa.
Suş no. 317



MHMB- % 2 glu, Flu, 24sa.
Suş no. 317

CLSI M44-A2 (Ağustos 2009): Candida-flu, vori, kaspo
Kalite kontrol aralıkları: flu, vori, kaspo, posa

Wild-type MIC distributions, epidemiological cutoff values and species-specific clinical breakpoints for fluconazole and *Candida*: Time for harmonization of CLSI and EUCAST broth microdilution methods

Drug Resistance Updates 13 (2010) 180–195

M.A. Pfaller[a,*], D. Andes[b], D.J. Diekema[a], A. Espinel-Ingroff[c], D. Sheehan[d], The CLSI Subcommittee for Antifungal Susceptibility Testing

Clinical breakpoints for voriconazole and *Candida* spp. revisited: review of microbiologic, molecular, pharmacodynamic, and clinical data as they pertain to the development of species-specific interpretive criteria ☆

Michael A. Pfaller[a,*,1], David Andes[b,1], Maiken C. Arendrup[c,1], Daniel J. Diekema[a,1], Ana Espinel-Ingroff[d,1], Barbara D. Alexander[e,1], Steven D. Brown[f,1], Vishnu Chaturvedi[g,1], Cynthia L. Fowler[h,1], Mahmoud A. Ghannoum[i,1], Elizabeth M. Johnson[j,1], Cynthia C. Knapp[k,1], Mary R. Motyl[l,1], Luis Ostrosky-Zeichner[m,1], Thomas J. Walsh[n,1]

Diagnostic Microbiology and Infectious Disease 70 (2011) 330–343

Evaluation of CLSI M44-A2 Disk Diffusion and Associated Breakpoint Testing of Caspofungin and Micafungin Using a Well-Characterized Panel of Wild-Type and *fks* Hot Spot Mutant *Candida* Isolates[▽]

Maiken Cavling Arendrup,[1]* Steven Park,[2] Steven Brown,[3] Michael Pfaller,[4] and David S. Perlin[2]

Unit of Mycology and Parasitology, Statens Serum Institut, Copenhagen, Denmark[1]; Public Health Research Institute, UMDNJ-New Jersey Medical School, Newark, New Jersey[2]; The Clinical Microbiology Institute, Wilsonville, Oregon[3]; and University of Iowa, Iowa City, Iowa[4]

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, May 2011, p. 1891–1895

Mediterr J Hematol Infect Dis 2014; 6; Open Journal System

Review Article

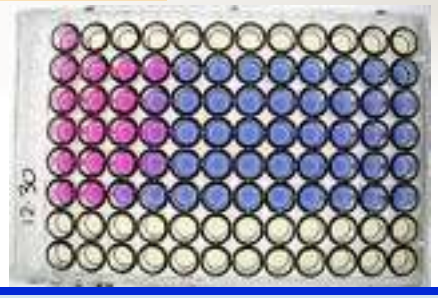
Antifungal Susceptibility Testing: Current Role from the Clinical Laboratory Perspective

Brunella Posteraro[1], Riccardo Torelli[2], Elena De Carolis[2], Patrizia Posteraro[3] and Maurizio Sanguinetti[2]

Table 1. Reference and non-reference methods for antifungal susceptibility testing of *Candida* and *Aspergillus* clinical isolates[a]

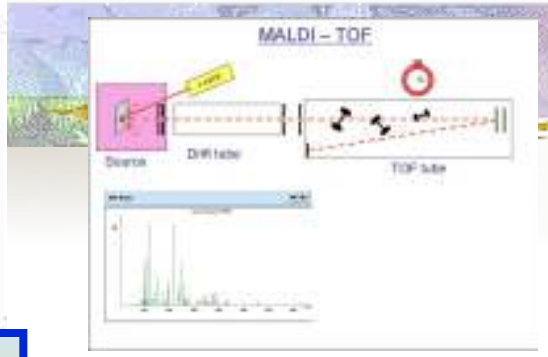
Characteristic	Standardized Methods		Commercial Methods			Novel Methods			
	CLSI	EUCAST	SYO	Etest	Vitek 2	FC	MALDI-TOF MS	IMC	4D plate
Suitability	Yeasts (M27-A3), molds (M38-A2)	Fermentative yeasts (EDef 7.2), molds (EDef 9.1)	Yeasts and molds	Yeasts and molds	Yeasts	*Candida* species	*Candida albicans*	*Aspergillus* species	*Aspergillus* species
Format[b]	BMD	BMD	BMD	Agar-based method	BMD (AST-YS06 cards)	Broth dilution	Broth dilution	Broth dilution	Agar dilution
Temperature	35 °C	35-37 °C	35-37 °C	35-37 °C	Instrument incubator	35 °C	37 °C	37 °C	37 °C
Incubation time	24-48 h	24-48 h	24-48 h	24-48 h	12-24 h	1-4 h	3 h	48 h	48 h
Reading	Visually	Visually/spectrophotometrically	Visually	Visually	Automatically	Fluorescence microscopy	Mass spectrometry	Isothermal microcalorimeter	Visually
Endpoint[c]	MIC, MEC (only for echinocandins)	MIC	MIC, MEC (only for echinocandins)	MIC	MIC	MFEC	CCI-measured spectral comparison	MHDC	No growth
Use (pros and cons)[d]	Detecting resistant isolates, but restricted to specialized laboratories	Detecting resistant isolates, but restricted to specialized laboratories	Routine testing of isolates, but categorization of resistant isolates not advised	Routine testing of isolates, but categorization of resistant isolates not advised	Routine testing of isolates, but categorization of resistant isolates not advised	Rapid detection of antifungal resistance, but today not applied to the routine clinical practice	Rapid detection of echinocandin resistance, but today not applied to the routine clinical practice	Potential detection of resistant isolates, but still in an infancy stage	Screening for potentially azole-resistant isolates, but confirmation by the reference method required

MİK
Strip Yöntemi



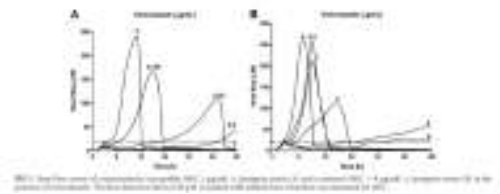
Kolorimetrik
Mikrodilüsyon
(Sensititre YeastOne®)

Tam otomatize
sistemler
(VITEK-2)

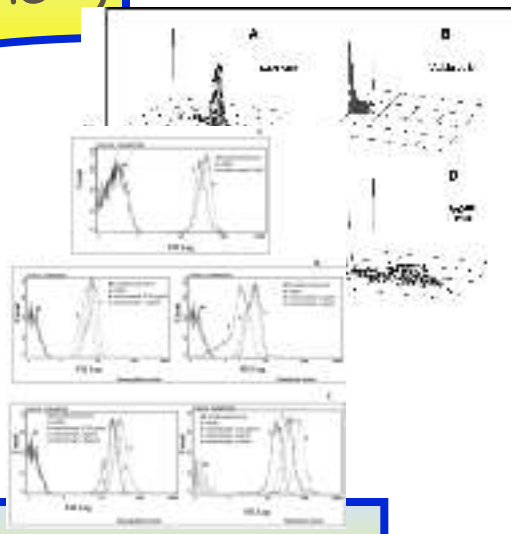


MALDI-TOF MS

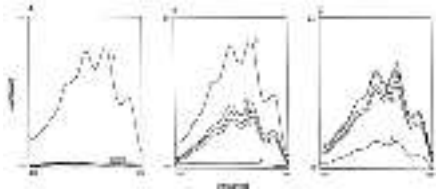
www.mpipz.mpg.de/44542/MALDI-TOF-TOF_MS_MS



İzotermal
mikrokalorimetre



"Flow" sitometre



Ergosterol
miktarının tayini

Arikan et al. DMID 2002; 43: 107; Pina-Vaz et al. JCM 2005; 43: 4674; Arthington-Skaggs et al. AAC 2002; 46: 2477 Arthington-Skaggs et al. AAC 2000; 44: 2081, Vale-Silva et al. Mycoses 2006; 49: 261

Önceki direnç sınır değerleri ile

Etest, Sensititre YeastOne – CLSI sonuçlarının karşılaştırılması

TABLE 5. Agreement by *Candida* species: Etest and Sensititre compared with CLSI M27-A2 broth microdilution reference method[a]

Test system	*Candida* species	No. of isolates	% Categorical agreement					% Essential agreement							
			5FC	FLC	ITC	VRC	Overall	5FC	FLC	ITC	VRC	PSC	AMB	CSP	Overall
Etest	*C. albicans*	94	97	98	94	100	97	93	98	97	93	100	99	89	96
	C. glabrata	38	100	55	74	76	76	100	82	89	89	95	100	90	92
	C. tropicalis	34	100	97	62	97	89	94	100	94	85	100	100	88	94
	C. parapsilosis	31	100	97	81	100	94	100	87	100	97	100	100	100	98
	C. krusei	5	20	40	0	100	40	100	40	80	100	100	100	100	89
	C. lusitaniae	8	100	88	88	100	94	100	100	100	100	100	100	100	100
	C. guillermondii	2	100	100	50	100	88	100	100	100	100	100	100	100	100
	Overall	212	97	88	80	95	90	96	92	95	92	99	99	92	95
Sensititre	*C. albicans*	94	99	97	100	100	99	96	96	100	82	NA	100	90	94
	C. glabrata	38	100	34	68	87	72	97	66	89	89	NA	100	97	90
	C. tropicalis	34	100	94	32	97	81	79	85	88	76	NA	100	79	85
	C. parapsilosis	31	100	90	48	100	85	87	48	100	90	NA	100	97	87
	C. krusei	5	80	40	80	100	75	100	100	100	100	NA	100	100	100
	C. lusitaniae	8	100	100	50	100	88	100	100	100	100	NA	100	100	100
	C. guillermondii	2	100	100	50	100	88	0	100	100	100	NA	100	100	83
	Overall	212	99	83	73	97	88	92	82	96	85	NA	100	92	91

[a] FLC, fluconazole; PSC, posaconazole; ITC, itraconazole; VRC, voriconazole; 5FC, 5 flucytosine; AMB, amphotericin B; CSP, caspofungin. NA, not applicable.

Çoğu minör hata

Azol – glabrata; Etest / Sensititre

Alexander et al. JCM 2007; 45: 698

Revize edilmiş, türe özgü direnç sınır değerleri ile

Candida – Kandin
CLSI ile Sensititre YeastOne

Comparison of the Sensititre YeastOne colorimetric antifungal panel with CLSI microdilution for antifungal susceptibility testing of the echinocandins against *Candida* spp., using new clinical breakpoints and epidemiological cutoff values ☆

M.A. Pfaller[a,b], V. Chaturvedi[c], D.J. Diekema[a,*], M.A. Ghannoum[d], N.M. Holliday[e], S.B. Killian[e], C.C. Knapp[e], S.A. Messer[a,b], A. Miskou[e], R. Ramani[c]

Diagnostic Microbiology and Infectious Disease 73 (2012) 365–368

Categorical agreement (CA) between Sensititre YeastOne antifungal panel MICs and 24-h CLSI BMD anidulafungin, caspofungin, and micafungin MICs for 580 isolates of *Candida* using new clinical breakpoints or epidemiological cutoff values.

Species (no. of isolates tested)	Antifungal agent	% of MICs by category[a,b]			CA%	% of errors[c]		
		S	I	R		VME	ME	Minor
C. albicans (174)	Anidulafungin	100.0	0.0	0.0	100.0	0.0	0.0	0.0
	Caspofungin	100.0	0.0	0.0	98.3	0.0	0.0	1.7
	Micafungin	100.0	0.0	0.0	100.0	0.0	0.0	0.0
C. glabrata (87)	Anidulafungin	95.4	3.4	1.2	93.1	1.1	0.0	5.8
	Caspofungin	83.9	11.5	4.6	89.7	1.1	1.1	8.1
	Micafungin	97.6	1.2	1.2	98.9	0.0	0.0	1.1
C. parapsilosis (90)	Anidulafungin	98.9	1.1	0.0	96.7	0.0	0.0	3.3
	Caspofungin	100.0	0.0	0.0	100.0	0.0	0.0	0.0
	Micafungin	100.0	0.0	0.0	100.0	0.0	0.0	0.0
C. tropicalis (73)	Anidulafungin	98.6	1.4	0.0	100.0	0.0	0.0	0.0
	Caspofungin	100.0	0.0	0.0	100.0	0.0	0.0	0.0
	Micafungin	98.6	0.0	1.4	100.0	0.0	0.0	0.0
C. krusei (81)	Anidulafungin	100.0	0.0	0.0	98.8	0.0	0.0	1.2
	Caspofungin	76.5	23.5	0.0	69.1	1.2	0.0	29.7
	Micafungin	100.0	0.0	0.0	100.0	0.0	0.0	0.0
C. lusitaniae (75)	Anidulafungin	100.0		0.0	100.0	0.0	0.0	0.0
	Caspofungin	100.0		0.0	100.0	0.0	0.0	0.0
	Micafungin	98.7		1.3	98.7	1.3	0.0	0.0
All *Candida* spp. (580)	Anidulafungin	99.1	0.7	0.2	98.3	0.2	0.0	1.5
	Caspofungin	94.1	5.0	0.9	93.6	0.3	0.2	5.9
	Micafungin	99.3	0.2	0.5	99.6	0.2	0.0	0.2

404 suş; benzer sonuçlar
Kategori uyumu:
%93.6 (kaspofungin)
%99.6 (mikafungin)
VME /ME < %1

Revize edilmiş, türe özgü direnç sınır değerleri ile

Candida – Flu&Vori
CLSI ile VITEK-2

Diagnostic Microbiology and Infectious Disease 77 (2013) 37–40

Comparison of the Vitek 2 yeast susceptibility system with CLSI microdilution for antifungal susceptibility testing of fluconazole and voriconazole against *Candida* spp., using new clinical breakpoints and epidemiological cutoff values

Michael A. Pfaller [a,*], Daniel J. Diekema [a], Gary W. Procop [b], Michael G. Rinaldi [c]

fluconazole (97.9%) and voriconazole (96.7%). Categorical agreement (CA) between the 2 methods was assessed using the new species-specific clinical breakpoints (CBPs): susceptible (S) ≤2 μg/mL, susceptible dose-dependent (SDD) 4 μg/mL, and resistant (R) ≥8 μg/mL for fluconazole and *Candida albicans*, *Candida tropicalis*, and *Candida parapsilosis* and ≤32 μg/mL (SDD), ≥64 μg/mL (R) for *Candida glabrata*; S ≤0.12 μg/mL, SDD 0.25–0.5 μg/mL, R ≥1 μg/mL for voriconazole and *C. albicans*, *C. tropicalis*, and *C. parapsilosis*, and ≤0.5 μg/mL (S), 1 μg/mL (SDD), ≥2 μg/mL (R) for *Candida krusei*. The epidemiological cutoff value (ECV) of 0.5 μg/mL for voriconazole and *C. glabrata* was used to differentiate wild-type (WT; MIC ≤ ECV) from non-WT (MIC > ECV) strains of this species. Due to the lack of CBPs for the less common species, the ECVs for fluconazole and voriconazole, respectively, were used for *Candida lusitaniae* (2 μg/mL and 0.03 μg/mL), *Candida dubliniensis* (0.5 μg/mL and 0.03 μg/mL), *Candida guilliermondii* (8 μg/mL and 0.25 μg/mL), and *Candida pelliculosa* (4 μg/mL and 0.25 μg/mL) to categorize isolates of these species as WT and non-WT. CA between the 2 methods was 96.8% for fluconazole and 96.5% for voriconazole with less than 1% very major errors and 1.3–3.0% major errors. The Vitek 2 yeast susceptibility system remains comparable to the CLSI BMD reference method for testing the susceptibility of *Candida* spp. when using the new (lower) CBPs and ECVs.

Candida & C. neoformans - Flu
CLSI ile VITEK-2

Revize edilmiş, türe özgü direnç sınır değerleri ile

Multicenter Evaluation of the New Vitek 2 Yeast Susceptibility Test Using New CLSI Clinical Breakpoints for Fluconazole

M. A. Pfaller,[a] D. J. Diekema,[a] G. W. Procop,[b] N. P. Wiederhold[c]

Journal of Clinical Microbiology p. 2126–2130 June 2014 Volume 52 Number 6

746 isolates of *Candida* species (702 isolates, 13 species) and 44 isolates of *C. neoformans* against fluconazole. Excellent essential agreement (EA) (within 2 dilutions) between the reference and Vitek 2 MICs was observed for fluconazole and *Candida* species (94.0%). The EA was lower for fluconazole and *C. neoformans* at 86.4%. The mean times to a result with the Vitek 2 test were 9.1 h for *Candida* species and 12.1 h for *C. neoformans*. Categorical agreement (CA) between the two methods was assessed by using the new species-specific CBPs. For less common species without fluconazole CBPs, the epidemiological cutoff values (ECVs) were used to differentiate wild-type (WT; MIC, ≤ECV) from non-WT (MIC, >ECV) strains. The CAs between the two methods were 92.0% for *Candida* species (0.3% very major errors [VME] and 2.6% major errors [ME]) and 84.1% for *C. neoformans* (4.5% VME and 11.4% ME). The updated Vitek 2 AF03 IUO yeast susceptibility system is comparable to the CLSI BMD reference method for testing the susceptibility of clinically important yeasts to fluconazole when using the new (lower) CBPs and ECVs.

Kat. Uyumu: %92
(Candida)
ME: %2.6
VME: %0.3

Comparison of Three Statistical Methods for Establishing Tentative Wild-Type Population and Epidemiological Cutoff Values for Echinocandins, Amphotericin B, Flucytosine, and Six *Candida* Species as Determined by the Colorimetric Sensititre YeastOne Method

Emilia Cantón,[a] Javier Pemán,[b] David Hervás,[c] Carmen Iñiguez,[d,e] David Navarro,[f] Julia Echeverría,[g] José Martínez-Alarcón,[h] Dionisia Fontanals,[i] Bárbara Gomila-Sard,[j] Buenaventura Buendía,[k] Luis Torroba,[l] Josefina Ayats,[m] Angel Bratos,[n] Ferran Sánchez-Reus,[o] Isabel Fernández-Natal,[p] and the FUNGEMYCA Study Group

December 2012 Volume 50 Number 12 Journal of Clinical Microbiology p. 3921–3926

Multicenter Study of Epidemiological Cutoff Values and Detection of Resistance in *Candida* spp. to Anidulafungin, Caspofungin, and Micafungin Using the Sensititre YeastOne Colorimetric Method

A. Espinel-Ingroff,[a] M. Alvarez-Fernandez,[b] E. Cantón,[c] P. L. Carver,[d] S. C.-A. Chen,[e] G. Eschenauer,[d,f] D. L. Getsinger,[g] G. M. Gonzalez,[h] N. P. Govender,[i] A. Grancini,[j] K. E. Hanson,[k] S. E. Kidd,[l] K. Klinker,[m] C. J. Kubin,[n] J. V. Kus,[o] S. R. Lockhart,[p] J. Meletiadis,[q] A. J. Morris,[r] T. Pelaez,[s] G. Quindós,[t] M. Rodriguez-Iglesias,[u] F. Sánchez-Reus,[v] S. Shoham,[w] N. L. Wengenack,[x] N. Borrell Solé,[y] J. Echeverria,[z] J. Esperalba,[aa] E. Gómez-G. de la Pedrosa,[bb] I. García García,[cc] M. J. Linares,[dd] F. Marco,[ee] P. Merino,[ff] J. Pemán,[gg] L. Pérez del Molino,[hh] E. Roselló Mayans,[ii] C. Rubio Calvo,[jj] M. Ruiz Pérez de Pipaon,[kk] G. Yagüe,[ll] G. Garcia-Effron,[mm] J. Guinea,[s] D. S. Perlin,[nn] M. Sanguinetti,[oo] R. Shields,[f] J. Turnidge[pp]

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AFD(T):
Doğru Uygulama ve Yarar Sağlayan Sonuç Bildirimi

- Primer direnç
- MİK dağılımları
- AFDT – Endikasyonlar
- Özel notlar