Kandida Enfeksiyonlarında Direnç Sorunu

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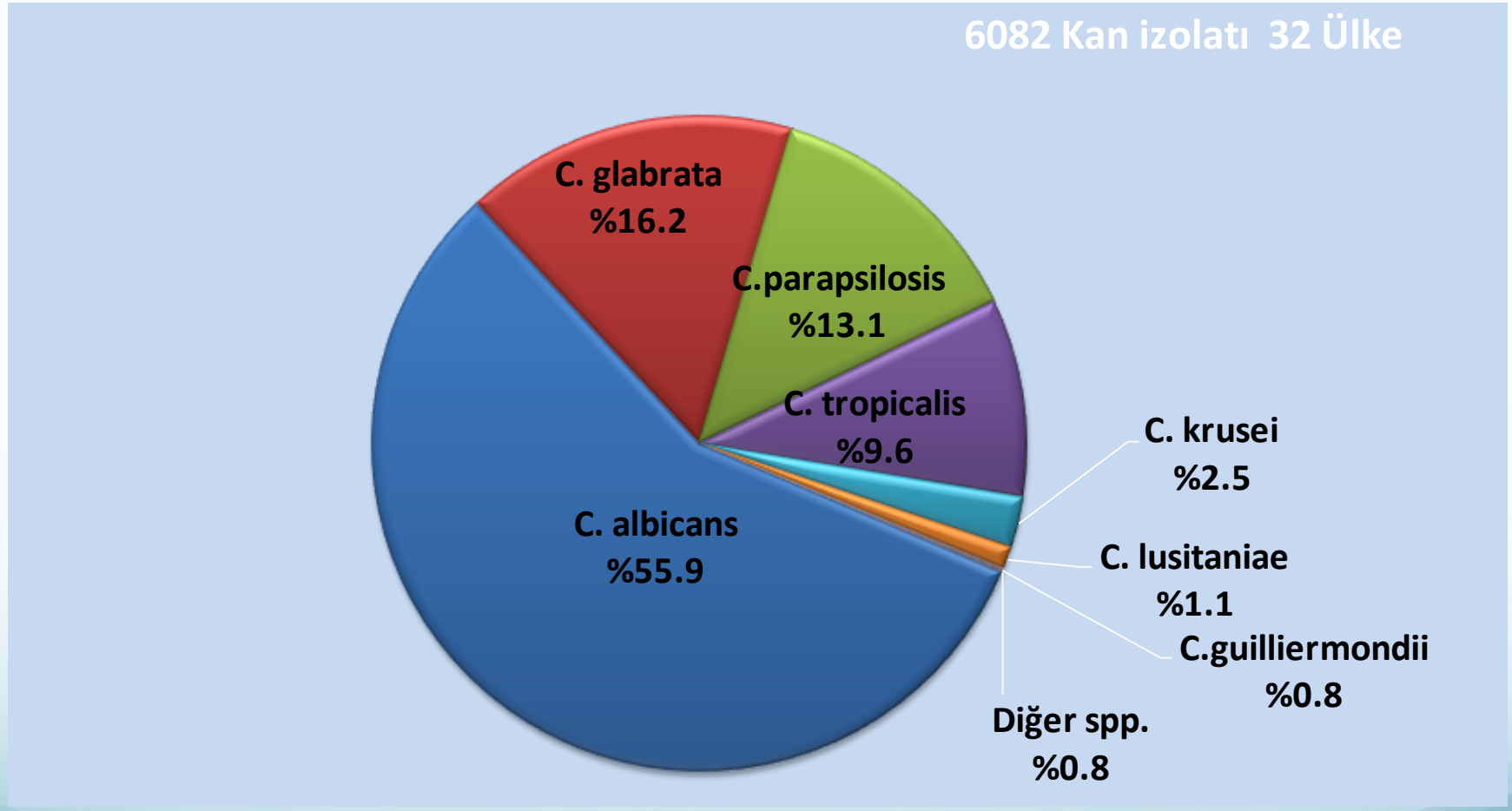
İnvaziv Fungal Enfeksiyonların Literatürde Rapor Edilen Oranları (%)

	İnvaziv Aspergilloz	Zigomikoz	İnvaziv Kandidiyaz	Diğer
Kemik İliği nakli	**43**	8	**28**	15
Solid Organ Nakli	18.8	2.3	**52.9**	19
Hematolojik Kanser	**33 - 69**	**-**	**13.5 - 44**	**-**
Yoğun Bakım	11	**-**	**79**	10

Kriengkauykiat J, Clin Epidem, 2011

Kandidemi Tür dağılımı – Dünya geneli



Pfaller, MA et al. *Clin Microbiol Infect*; 2004

Kandida türlerinin dağılımı

2008-2009, SENTRY

Table 2

Species distribution of *Candida* bloodstream infection isolates from Intensive Care Unit (ICU) and non-ICU locations.

Species	*n* (%) of each species according to origin	
	ICU (*N* = 779)	Non-ICU (*N* = 973)
C. albicans	393 (50.4)	461 (47.4)
C. glabrata	136 (17.5)	176 (18.1)
C. parapsilosis	118 (15.1)	184 (18.9)
C. tropicalis	82 (10.5)	93 (9.6)
C. krusei	16 (2.1)	20 (2.1)
Miscellaneous[a]	34 (4.4)	39 (4.0)

[a] Miscellaneous species including *C. lusitaniae* (31 isolates), *C. dubliniensis* (16 isolates), *C. guilliermondii* (8 isolates), *C. kefyr* (6 isolates), *C. famata* and *C. lipolytica* (3 isolates each) and *C. rugosa*, *C. sake* and *C. pelliculosa* (2 isolates each).

Pfaller MA, IJAA, 2011

2012-2015 SENTRY *Kandida* dağılımı-MÜTF

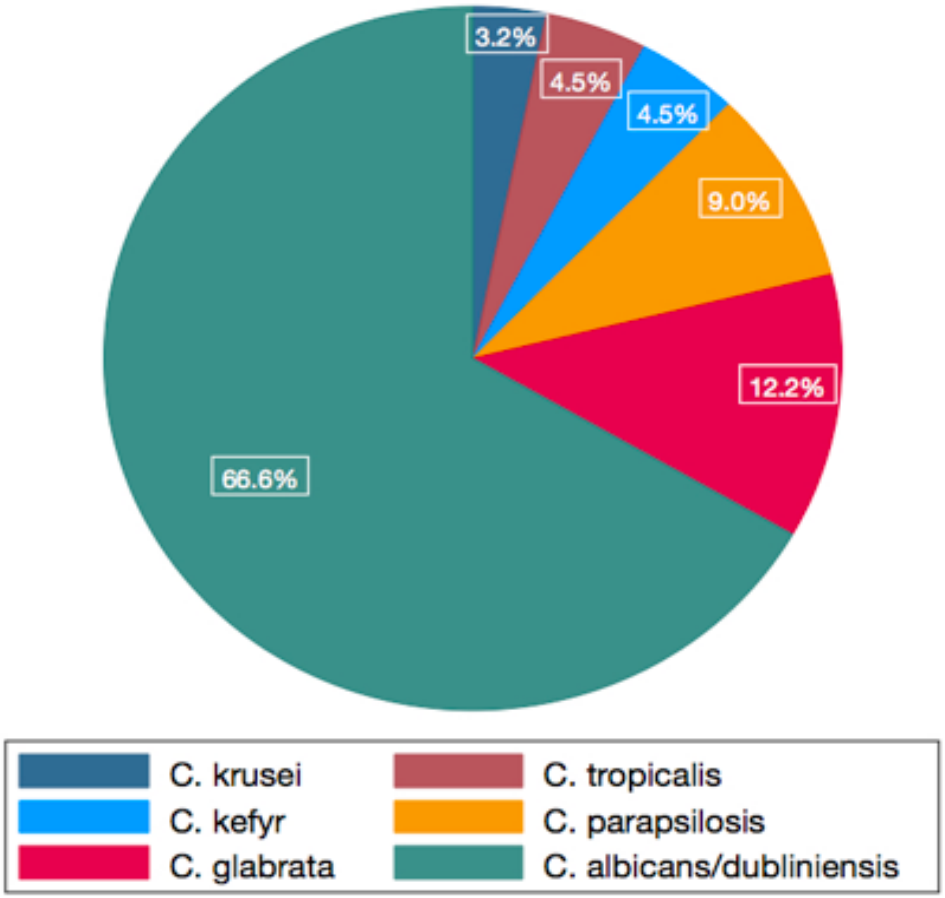


Figure 2. Proportions of Candida species tested for susceptibility by year (2012-2015)

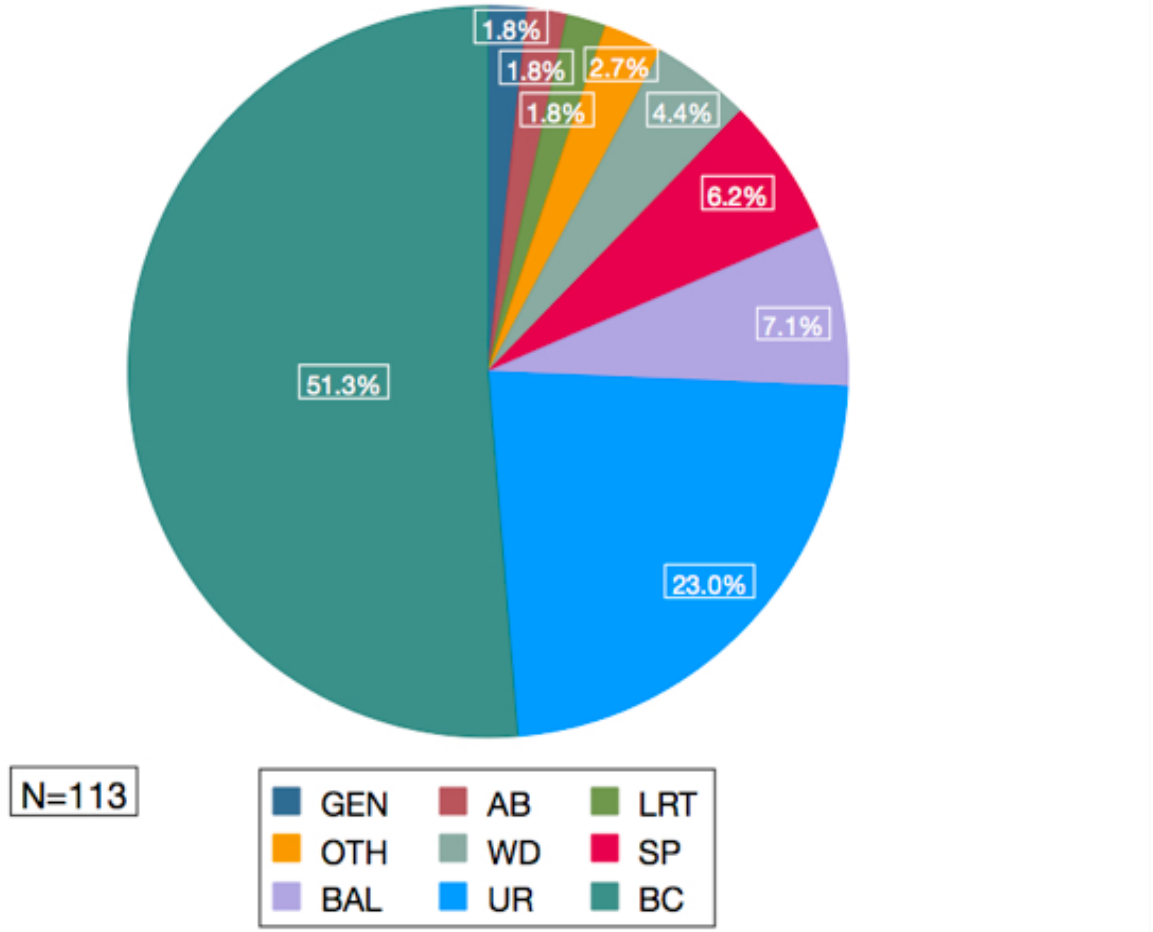
2012-2015 SENTRY *Kandida* dağılımı

Table 1. Candida species tested for susceptibility (2012-2015)

Species	2012	2013	2014	2015	Total
C. albicans/dubliniensis	23	40	16	25	104
C. glabrata	7	0	11	1	19
C. parapsilosis	5	0	6	3	14
C. tropicalis	0	0	2	5	7
C. kefyr	0	1	4	2	7
C. krusei	3	0	1	1	5
Number of isolates tested per year	38	41	40	37	156

Figure 1. Candida species tested for susceptibility (2012-2015)

Figure 3. Source of Candida those underwent susceptibility testing (proportion)



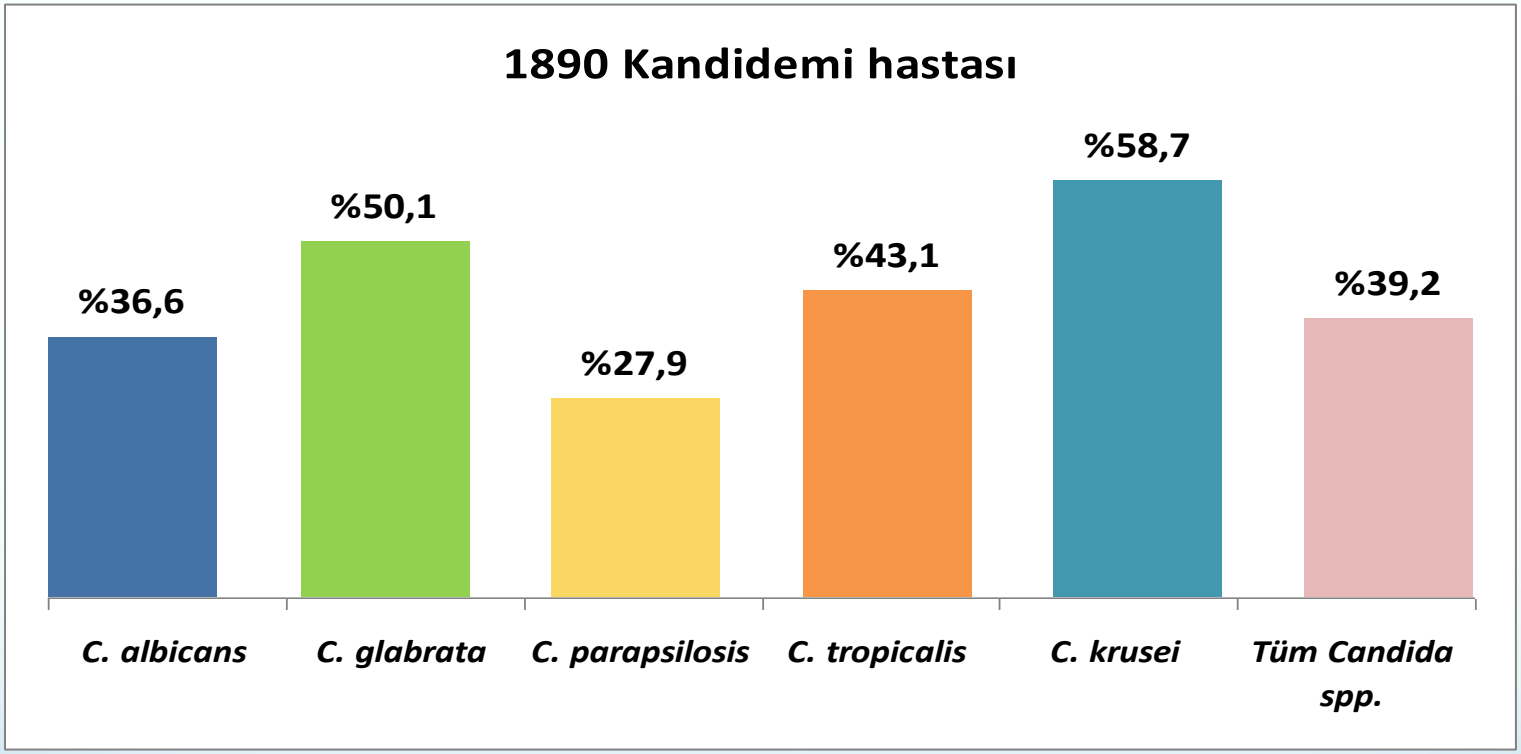
Kandidemi: Dördüncü En Sık ve En Mortal

Table 1. Rank order of nosocomial bloodstream pathogens and the associated crude mortality among 49 hospitals throughout the United States.

Rank	Pathogen	No. of isolates	%	Crude mortality (%)
1	Coagulase-negative staphylococci	3,908	31.9	21
2	*Staphylococcus aureus*	1,928	15.7	25
3	Enterococci	1,354	11.1	32
4	*Candida* species	934	7.6	40
5	*Escherichia coli*	700	5.7	24
6	*Klebsiella* species	662	5.4	27
7	*Enterobacter* species	557	4.5	28
8	*Pseudomonas* species	542	4.4	33
9	*Serratia* species	177	1.4	26
10	Viridans streptococci	173	1.4	23

Edmond, Clin İnfect Dis 1999

Kandida Türlerine Göre Mortalite İlişkisi



Wisplinghoff H et al. *Clin Infect Dis.* 2004; 39: 309-317.

İnvazif kandidiyazis mortalite

- Atfedilen mortalite %30-40
- Kandidaya bağlı septik şokta uygun odak kontrolü yapılmadığı veya 24 saat içinde antifungal başlanmadığı taktirde mortalite %100
- Hemen uygun antifungal başlanması ile mortalitede %50 azalma

Clin Practice Guideline for the Management of Candidiazis; 2016 update

Antifungaller ve *Kandida* Duyarlılıkları

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	**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.
Isavuconazole	IE	IE	IE	IE	IE	IE	IE	IE	IE	IE	IE	IE	IE	IE	
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	

EUCAST Version 8.0, valid from 2015-11-16

Antifungaller ve *Kandida* Duyarlılıkları

Candida Organism	Antifungal Agent	S	SDD	I	R
C. albicans	Fluconazole	≤2	4		≥8
	Itraconazole	≤0.12	0.25–0.5		≥1
	Voriconazole	≤0.12		0.25–0.5	≥1
	Posaconazole				
	Anidulafungin	≤0.25		0.5	≥1
	Caspofungin	≤0.25		0.5	≥1
	Micafungin	≤0.25		0.5	≥1
C. glabrata	Fluconazole		32		≥64
	Itraconazole				
	Voriconazole				
	Posaconazole				
	Anidulafungin	≤0.12		0.25	≥0.5
	Caspofungin	≤0.12		0.25	≥0.5
	Micafungin	≤0.06		0.12	≥0.25
C. parapsilosis	Fluconazole	≤2	4		≥8
	Itraconazole				
	Voriconazole	≤0.12		0.25–0.5	≥1
	Posaconazole				
	Anidulafungin	≤2		4	≥8
	Caspofungin	≤2		4	≥8
	Micafungin	≤2		4	≥8
C. tropicalis	Fluconazole	≤2	4		≥8
	Itraconazole				
	Voriconazole	≤0.12		0.25–0.5	≥1
	Posaconazole				
	Anidulafungin	≤0.25		0.5	≥1
	Caspofungin	≤0.25		0.5	≥1
	Micafungin	≤0.25		0.5	≥1
C. krusei	Fluconazole				
	Itraconazole				
	Voriconazole	≤0.5		1	≥2
	Posaconazole				
	Anidulafungin	≤0.25		0.5	≥1
	Caspofungin	≤0.25		0.5	≥1
	Micafungin	≤0.25		0.5	≥1

Antifungaller ve *Kandida* Duyarlılıkları

Table 2 Clinical breakpoints (CBPs) for *Candida* versus fluconazole, voriconazole and echinocandins as determined by CLSI and EUCAST broth microdilution methods

Method / agent / species	Incubation time, *h*	MIC by category, *μg/mL*			
		Susceptible	Susceptible dose-dependent	Intermediate	Resistant
CLSI					
Fluconazole[a]	24	≤2	4	–	≥8
C. glabrata	24	–	32	–	≥64
Voriconazole[b]	48	≤1	2	–	≥4
Echinocandins[c]	24	≤0.25	–	0.5	≥1
C. parapsilosis	24	≤2	–	4	≥8
C. guilliermondii	24	≤2	–	4	≥8
Micafungin[c]					
C. glabrata	24	≤0.06	_	0.12	≥0.25
EUCAST[d]					
Fluconazole	24	≤2	–	4	>4
Voriconazole	24	≤0.12	–	–	>0.12

CLSI Clinical and Laboratory Standards Institute, *EUCAST* European Committee on Antibiotic Susceptibility Testing, *MIC* minimal inhibitory concentration

[a] CLSI fluconazole CBPs are species-specific and apply to *C. albicans*, *C. parapsilosis*, and *C. tropicalis*, as well as *C. glabrata*. *C. krusei* is intrinsically resistant to fluconazole; MICs determined at 24 h [17••]

[b] CLSI voriconazole CBPs are not species-specific and this adjustment is expected in the near future; MICs at 48 h [2•, 3]

[c] CLSI echinocandin (anidulafungin, caspofungin, and micafungin) CBPs are species-specific and apply to *C. albicans*, *C. tropicalis*, and *C. krusei*. CLSI micafungin CBPs for *C. glabrata* are lower, but anidulafungin and caspofungin CBPs are the same as for the former three species; MICs determined at 24 h [31••]

[d] EUCAST (EDef 7.1) fluconazole and voriconazole CBPs are species-specific values and apply to *C. albicans*, *C. tropicalis*, and *C. parapsilosis*. No CBPs for *C. glabrata* and *C. krusei* were established because of insufficient data and because those species were not considered good targets for voriconazole therapy [7, 8]

Ana Espinel-Ingroff et al. Curr Fungal Infect Rep, (2010)4:186–195

Kandida türlerinde Ekinokandinlerin karşılaştırılması

	Anidulafungin		Micafungin		Caspofungin	
***Candida* spp.**	**MIC_{50}**	**MIC_{90}**	**MIC_{50}**	**MIC_{90}**	**MIC_{50}**	**MIC_{90}**
albicans	0.03	0.03	0.015–0.03	0.03	0.03–0.5	0.06–1.0
glabrata	0.03	0.13	0.015–0.03	0.015–0.06	0.03–1.0	0.06–2.0
tropicalis	0.03	0.13	0.03	0.06	0.12–0.5	0.25–1.0
dubliniensis	0.03	0.06	0.03	0.033	0.25–0.5	0.5
krusei	0.06	0.13	0.06–0.13	0.06–0.25	0.12–2.0	0.25–2.0
lusitaniae	0.06	0.25	0.06	2.0	0.5–1.0	1.0–2.0
parapsilosis	2.0	2.0	1.0	2.0	1.0–2.0	1.0–4.0
guilliermondii	ND	1.0	ND	0.5	2.0–>8.0	2.0–>8.0

MIC_{50} or MIC_{90} = minimum inhibitory concentration for 50% or 90%, respectively, **(µg/mL)**

Cappellety D, et al. Pharmacotherapy 2007;27:369–68

2012-2015 SENTRY *Kandida* azol duyarlılığı-MÜTF

Tablo 2. Candida türlerinin azol duyarlılıkları

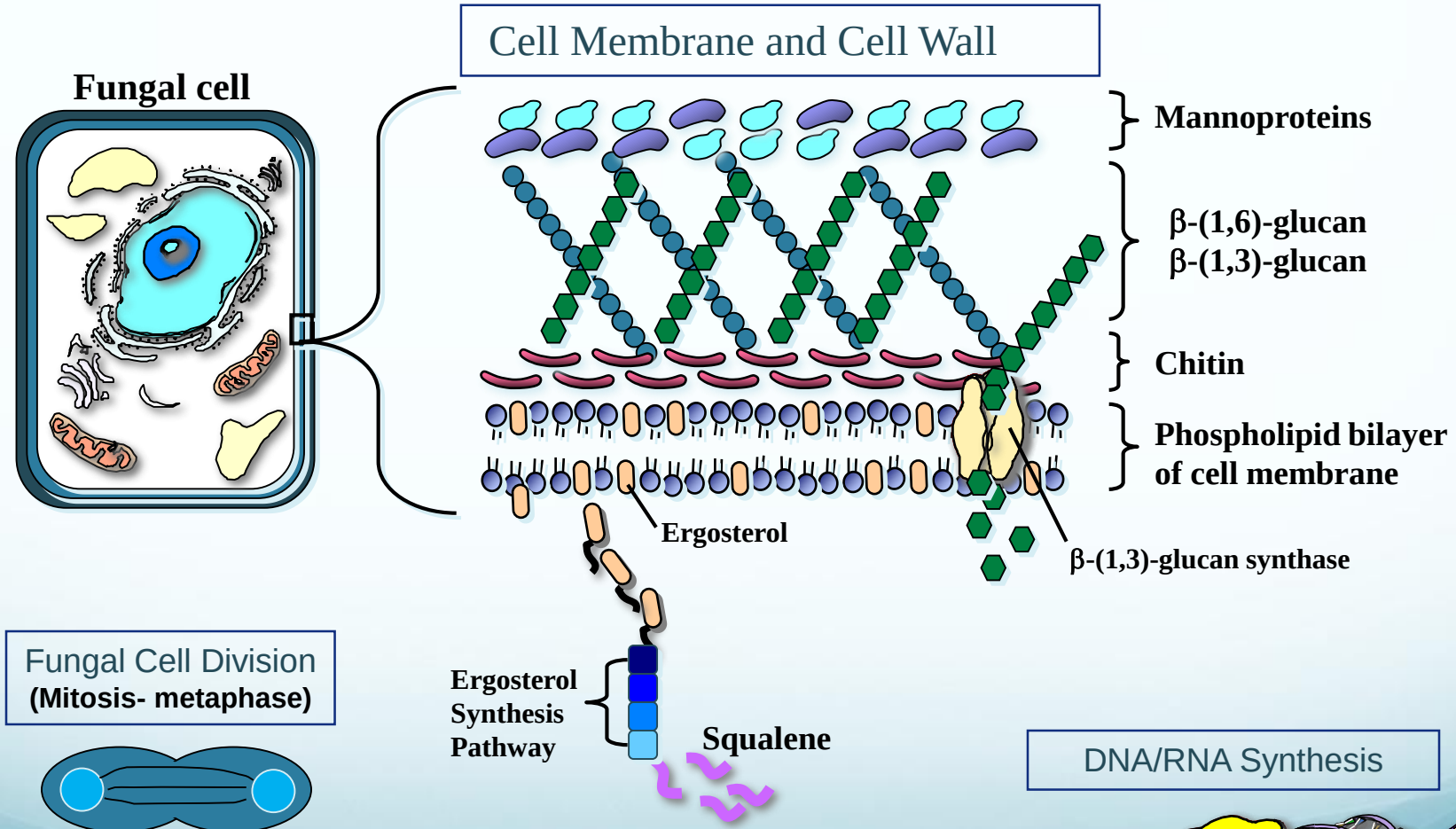
Türler	Antifungal	Duyarlılık Sonuçları, N (%)				
		EUCAST		CLSI		
		Duyarlı	Dirençli	Duyarlı	DBD	Dirençli
C.albicans/dupliniensis	Flukonazol	104/104(100)	0	104/104(100)	0	0
	İtrakonazol	53/63 (84.1)	10/63(15.9)	VY	VY	VY
	Posakonazol	103/104 (99)	1/104 (1)	VY	VY	VY
	Vorikonazol	104/104(100)	0	104/104(100)	0	0
C.glabrata	Flukonazol	18/19(94.7)	1/19(5.3)	0	18/19(94.7)	1/19(5.3)
	İtrakonazol	7/7(100)	0	VY	VY	VY
	Posakonazol	VY	VY	VY	VY	VY
	Vorikonazol	18/19(94.7)	1/19(5.3)	VY	VY	VY
C.parapsilosis	Flukonazol	14/14(100)	0	14/14(100)	0	0
	İtrakonazol	1/5(20)	4/5(80)	VY	VY	VY
	Posakonazol	9/14(64.3)	5/14(15.7)	VY	VY	VY
	Vorikonazol	14/14(100)	0	14/14(100)	0	0
C.tropicalis	Flukonazol	7/7(100)	0	7/7(100)	0	0
	İtrakonazol	U	U	VY	VY	VY
	Posakonazol	6/7(85.7)	1/7(14.3)	VY	VY	VY
	Vorikonazol	7/7(100)	0	7/7(100)	0	0
C.kefyr	Flukonazol	7/7(100)	0	VY	VY	VY
	İtrakonazol	VY	VY	VY	VY	VY
	Posakonazol	VY	VY	VY	VY	VY
	Vorikonazol	VY	VY	VY	VY	VY
C.krusei	Flukonazol	U	U	U	U	U
	İtrakonazol	3/3(100)	0	VY	VY	VY
	Posakonazol	VY	VY	VY	VY	VY
	Vorikonazol	5/5(100)	0	5/5(100)	0	0

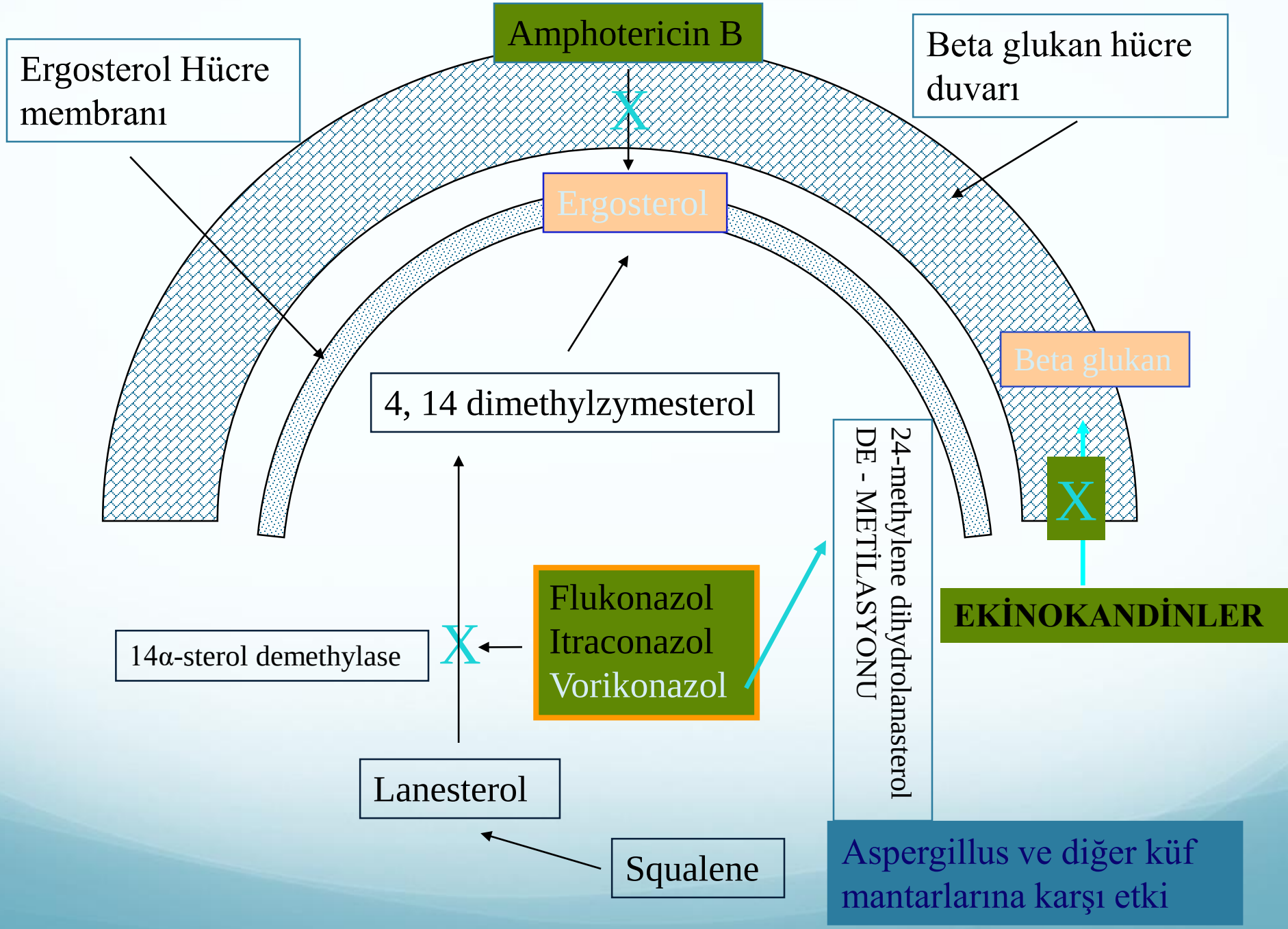
2012-2015 SENTRY *Kandida* ekinokandin duyarlılığı-MÜTF

Tablo 3. Candida türlerinin ekinokandin duyarlılıkları

Türler	Antifungal	Duyarlılık Sonuçları, N (%)		
		Duyarlı	DBD	Dirençli
C.albicans/dupliniensis	Amfoterisin B	VY	VY	VY
	Anidulofungin	104/104(100)	0	0
	Kaspofungin	104/104(100)	0	0
	Mikafungin	104/104(100)	0	0
C.glabrata	Amfoterisin B	VY	VY	VY
	Anidulofungin	19/19(100)	0	0
	Kaspofungin	19/19(100)	0	0
	Mikafungin	19/19(100)	0	0
C.parapsilosis	Amfoterisin B	VY	VY	VY
	Anidulofungin	12/14(85.7)	2/14(14.3)	0
	Kaspofungin	14/14(100)	0	0
	Mikafungin	14/14(100)	0	0
C.tropicalis	Amfoterisin B	VY	VY	VY
	Anidulofungin	7/7(100)	0	0
	Kaspofungin	7/7(100)	0	0
	Mikafungin	7/7(100)	0	0
C.kefyr	Amfoterisin B	VY	VY	VY
	Anidulofungin	VY	VY	VY
	Kaspofungin	VY	VY	VY
	Mikafungin	VY	VY	VY
C.krusei	Amfoterisin B	VY	VY	VY
	Anidulofungin	5/5(100)	0	0
	Kaspofungin	5/5(100)	0	0
	Mikafungin	5/5(100)	0	0

Antifungal drugs exploit cell properties unique to fungal pathogens - thereby drugs are selectively toxic to pathogen but not to human host.




Amphotericin B
Ergosterol Hücre membranı
Beta glukan hücre duvarı
X
Ergosterol
Beta glukan
4, 14 dimethylzymesterol
X
EKİNOKANDİNLER
24-methylene dihydrolanasterol
DE - METİLASYONU
Flukonazol
Itraconazol
Vorikonazol
14α-sterol demethylase
X
Lanesterol
Squalene
Aspergillus ve diğer küf mantarlarına karşı etki

Kandida Türlerinde Direnç Gelişimi: Epidemiyoloji

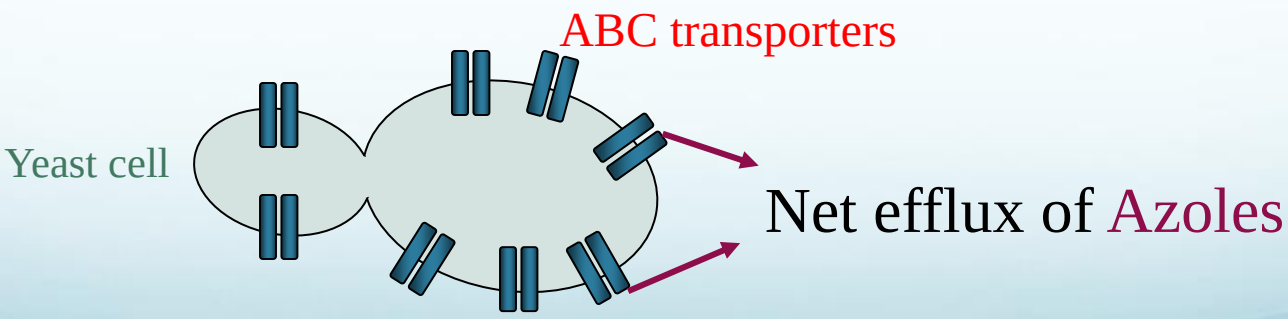
- Azol Direnci
  - Flukonazolun tedavi ve profilaksi amaçlı yaygın kullanımı
  - Azol dirençli *C.albicans* ve *C.glabrata* artışı
  - İmmünkompromize hastalarda non-albicans artışı
- Ekinokandin direnci
  - İntrensek olarak *C.parapsilosis* ve *C.gulliermondi* MİK değerlerinin yüksek olması
  - Tedavi altında MİK değerlerinin yükselmesi, edinilmiş direnç
- Poliyen direnci
  - 50 yılı aşan kullanıma rağmen direnç düşük
  - *C.krusei* ve *C.glabrata* 'da hafif MİK artışı

Kanafani (2008); Arthrington-Skaggs (2010); Pfaller (2012); Vandeputte (2012)

Antifungal direnç mekanizmaları

Azol direnci

- Uzamış azol tedavisi
- Mekanizma; ERG11 gen mutasyonu (lanosterol demetilaz)
  ABC transporter tarafından azol eflux
  Artmış ERG11 sekresyonu
  Sterol sentezinde değişiklik

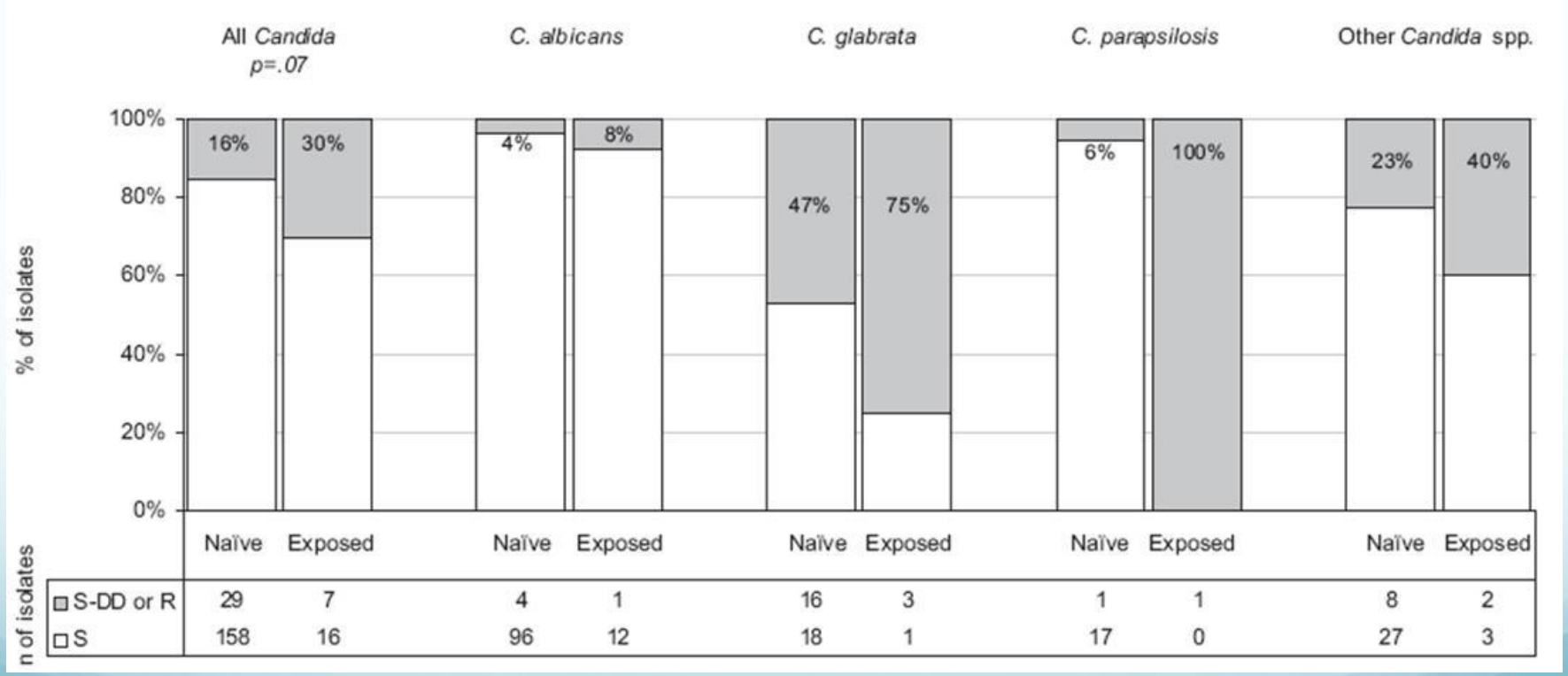


Önceden Azol Kullanımı ve Flukonazol Direnç İlişkisi

- Avustralya çalışması (Slavin et al, 2010)
  - 138 kandidemi epizodu
  - Önceden azol kullanımı; OR, 2.9; 95% CI, 1.33–61; P = 0.007
  - Son 14 günde azol: OR, 3.4; 95% CI, 1.0–11.3; P = 0.05

- İspanya çalışması (Garnacho-Montero et al.2010)
  - 226 kandidemik hasta
  - Azol öyküsü - direnç: OR, 5.09; 95% CI, 1.66–15.6; P = 0.004

Naif ve önceden flukonazol kullanmış hastalarda kandida izolatlarının flukonazol duyarlılıkları



C. glabrata – Flukonazol vs Vorikonazol Çapraz Direnci

TABLE 12. Resistance to fluconazole and voriconazole among isolates of *C. glabrata* from four geographic regions, 2001 to 2003[a]

Region	Antifungal agent	No. of isolates tested	% Resistant
Asia-Pacific	Fluconazole	1,859	10.6
	Voriconazole	1,727	4.1
Europe	Fluconazole	4,962	16.5
	Voriconazole	4,801	5.6
Latin America	Fluconazole	940	13.2
	Voriconazole	910	5.4
North America	Fluconazole	1,276	18.0
	Voriconazole	1,278	9.0

[a] Fluconazole and voriconazole disk diffusion testing performed in accordance with CLSI guideline M44-A (170). Data are compiled from the study of Pfaller et al. (221).

Flukonazol dirençli *C. glabrata* izolatlarında diğer antifungallerin etkinliği

Antifungal agent	No. of strains for which MIC (μg/ml) was:											
	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64
Amphotericin B				1	16	19	10					
Flucytosine		21	24	1								
Posaconazole				1		1	18	8	4	14		
Ravuconazole		1				3	10	21	10	1		
Voriconazole		1				5	16	20	4			
Caspofungin[a]	22	21	2	1								

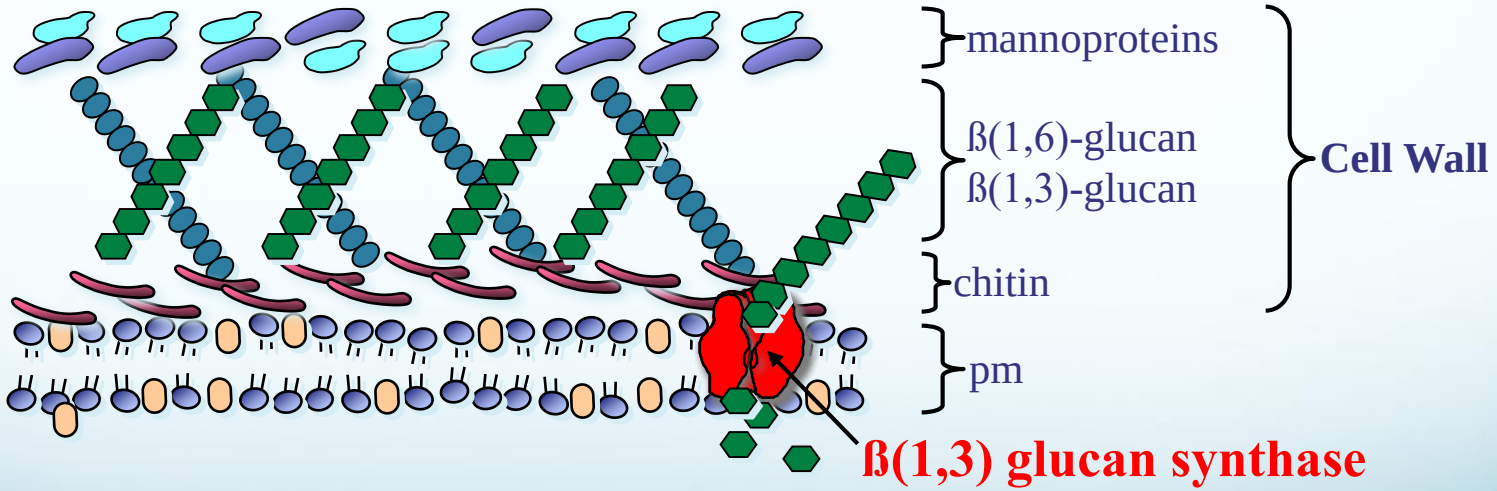
Pfaller, JCM, 2004

Antifungal direnç mekanizmaları

Ekinokandin direnci

- 1,3 B glukan sentaz enzimini kodlayan Fks1/Fks2 genlerinde spesifik nokta mutasyonları

(*Antimicrob. Agents Chemother*. (2005) 49, 3264; *Med. Mycol*. (2005) 43, 299)



Ekinokandinler – Etki Mekanizması

Ekinokandinler **B-1-3 glukan sentez** enzimi üzerinden hücre duvarına beta glukan eklenmesini inhibe edip hücre lizisine yol açarlar

CDC Surveyans datasına göre;

- Amerika'da 4 ayrı coğrafi bölge
- 80 hastane, 1385 *C.glabrata* izolatı
- Ekinokandin non-susceptible *C. glabrata*

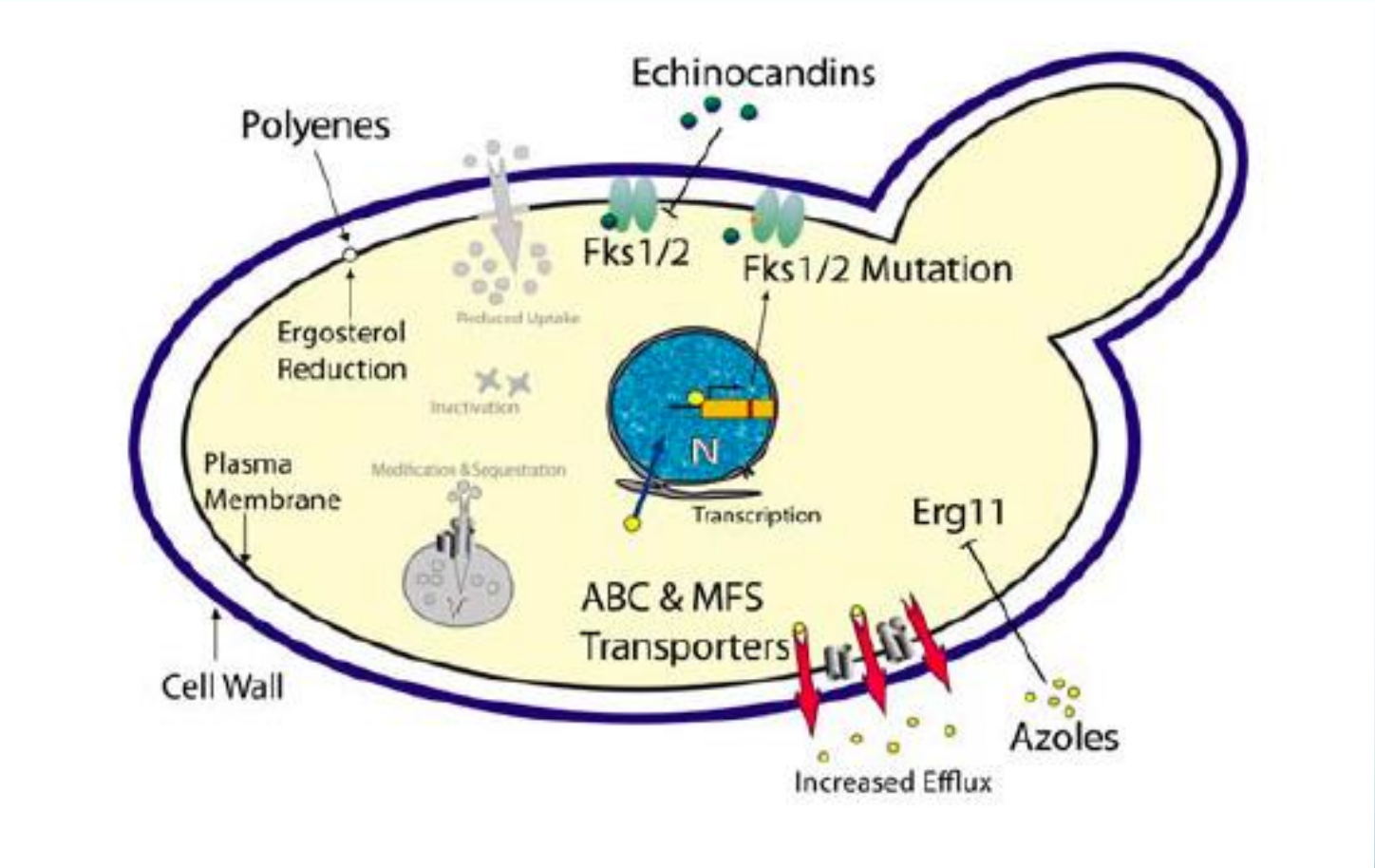
  2008 yılında %4.2

  2014 yılında %7.8

Vallabhaneni S et al. Infect Dis. 2015;2;ofv 163

Species	Antifungal agent	% of isolates resistant to each antifungal[a]	
		ICU	
		N[b]	%R
C. albicans	Anidulafungin	393	0.3
	Caspofungin	393	0.3
	Micafungin	393	0.3
	Fluconazole	393	0.0
	Posaconazole	393	0.0
	Voriconazole	393	0.0
C. glabrata	Anidulafungin	136	2.2
	Caspofungin	136	2.2
	Micafungin	136	2.2
	Fluconazole	136	5.9
	Posaconazole	136	4.4
	Voriconazole	136	5.9
C. parapsilosis	Anidulafungin	118	0.0
	Caspofungin	118	0.0
	Micafungin	118	0.0
	Fluconazole	118	6.8
	Posaconazole	118	0.0
	Voriconazole	118	0.0
C. tropicalis	Anidulafungin	82	0.0
	Caspofungin	82	0.0
	Micafungin	82	0.0
	Fluconazole	82	4.9
	Posaconazole	82	1.2
	Voriconazole	82	4.9
C. krusei[c]	Anidulafungin	16	0.0
	Caspofungin	16	6.3
	Micafungin	16	0.0
	Posaconazole	16	0.0
	Voriconazole	16	0.0

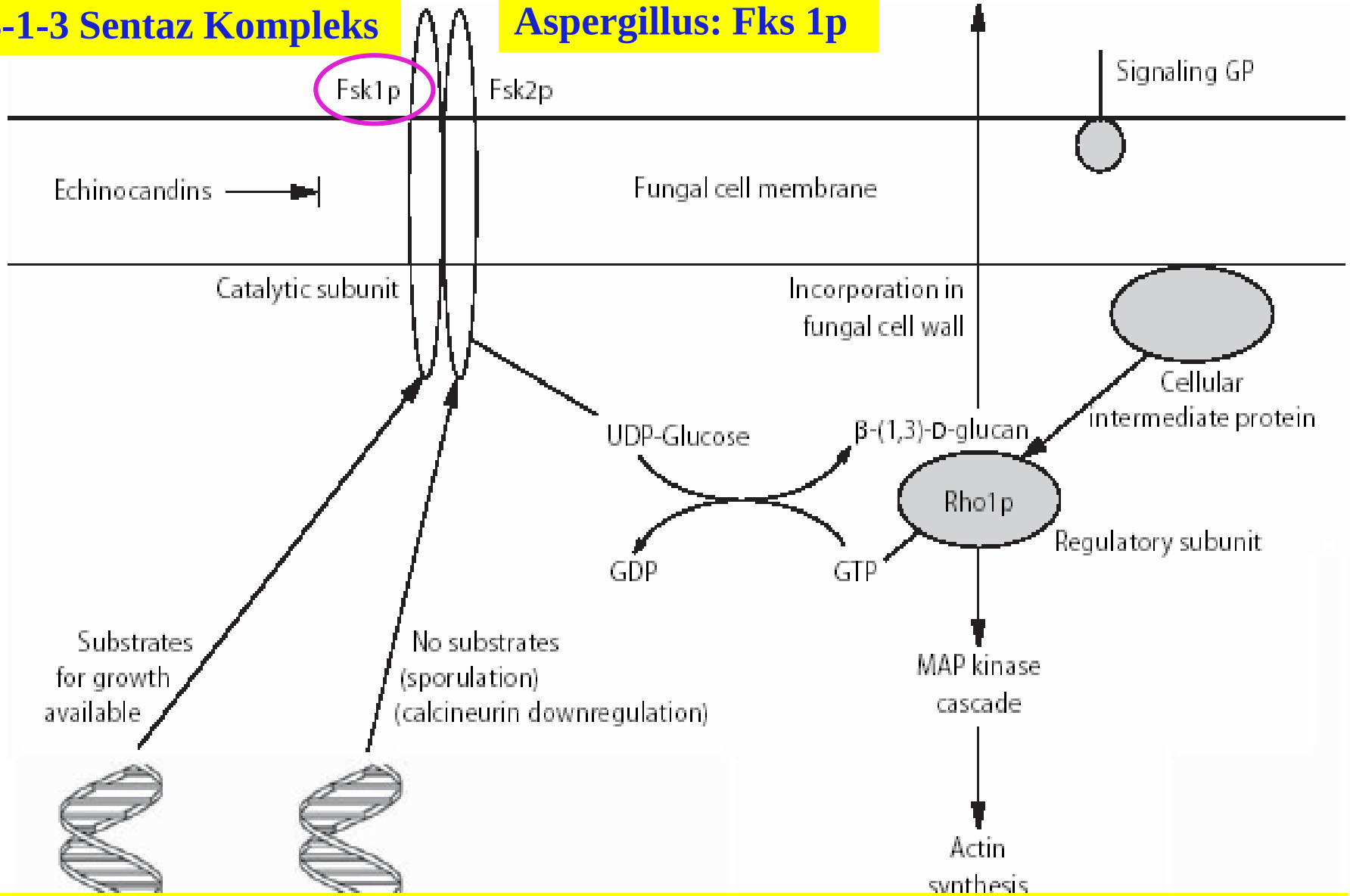
Antifungal direnç mekanizmaları



Michael Tscherner et al.Pharmaceuticals 2011

B-1-3 Sentaz Kompleks

Aspergillus: Fks 1p



Diğer antifungallerden farklı etki mekanizması sayesinde çapraz direnç görülme ihtimali yok

Çoğul İlaç Dirençli Kandida

TABLE 16. Clinical and in vitro resistance to echinocandins in patients with candidiasis[a]

Study	Species	Infection type	No. of isolates	Echinocandin MIC range (μg/ml)[b]	Coresistance
Moudgal et al. (167)	*C. parapsilosis*	Endocarditis	6	2–>16*	Caspofungin, micafungin, azoles
Dodgson et al. (63)	*C. glabrata*	Candidemia	15	0.12–>8*	Caspofungin, azoles
Krogh-Madsen et al. (120)	*C. glabrata*	Candidemia	4	0.5–>8*	Caspofungin, amphotericin B, azoles
Hernandez et al. (102)	*C. albicans*	Esophagitis	3	0.25–>64*	Caspofungin, azoles
Laverdiere et al. (126)	*C. albicans*	Esophagitis	4	0.03–2†	Micafungin, caspofungin, azoles

[a] All patients were treated with caspofungin, with the exception of those in the study of Laverdiere et al. (126) (micafungin).
[b] Symbols: *, caspofungin MICs; †, micafungin MICs.

Duke University Medical Center

- 313 *C.glabrata* kan izolatı
- 2001/2010 ekinokandin R %4.9 ➔ %12.3
- 2001/2010 flukonazol R %18 ➔ %30

- 78 flukonazol R izolat

  %14.1 ≥1 ekinokandin R

Barbara D. Alexander et al. Clin Infect Dis, 2013

SENTRY

- 2006-2010 yıllarında 1669 *C.glabrata* kan izolatı
- 162 (%9.7) flukonazol R ve bunların

  %98.8 non-susceptible vorikonazol

2001-2004 yıllarında 110 flukonazol R *C.glabrata* izolatında ekinokandin direnci yok

  %8 mikafungin R

- %11.1 (18) flukonazol R izolat ≥1 ekinokandin R

M. A. Pfaller et al.Journal of Clin Micr, 2011

Çoklu direncin sebebi ne?

- Bilinmiyor

- Hastanın multipl antifungal kullanımı ?
- *C.glabrata*'nın haploid genomu ?
- Altta yatan immunsupresyon ?
- Safra %30, asit %15 ➔ subinhibitör konsant. ?

Azol ve Ekinokandin Kullanımının Etkileri

- Fransa, 2441 vaka
- Son 30 günde kaspofungin veya flukonazol

- Kaspofungin: 61
- *C glabrata, C parapsilosis*

- Flukonazol: 159
- *C glabrata ve C krusei*

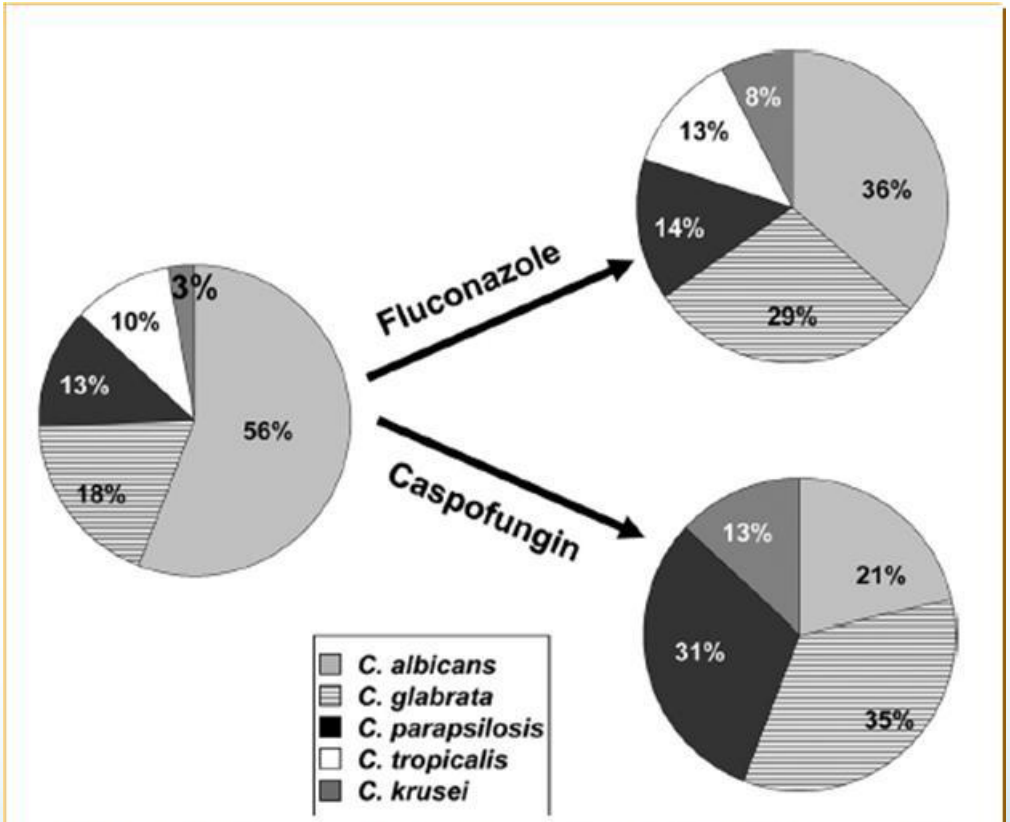


FIG. 2. Proportion of the five major *Candida* species responsible for fungemia in patients with (n = 159) or without (n = 2,289) prior exposure to fluconazole (P = 0.001) or with (n = 61) or without (n = 2,387) prior exposure to caspofungin ($P < 0.001$) (incident episodes and recurrences are included).

Lortholary et al. AAC, 2011

Ne Zaman Antifungal Duyarlılık Testi Yapılmalı

- Rutin yapılması şart değil:
- *Candida* infeksiyonlarında duyarlılık testi endikasyonları:
  - Ünitedeki duyarlılık paternlerinin belirlenmesi
  - Araştırma amaçlı
    - Yeni antifungal
    - Antifungal duyarlılık – klinik etkinlik araştırmaları
  - İnvazif fungal infeksiyon (steril bölgeden izole)
  - *C. glabrata* üremesi durumunda
  - Beklenmeyen klinik başarısızlık
  - Ünitenin empirik tedavi protokolünün belirlenmesi
- Küf mantarlarında bu konu tartışmalı

Ne yapmalı

CDC

- Çok merkezli *Kandida* surveyans programı oluşturarak antifungal duyarlılıkları test etmek

Enfeksiyon Kontrol ekibi

- Antibiyotik yönetim programlarının parçası olarak antifungal kullanımını değerlendirmek
- El hijyeni, kateter ilişkili enfeksiyonlardan koruma ve çevresel önlemlere uyumu sağlamak

CDC, Antifungal Resistance, 18 August 2016

Ne yapmalı

Doktorlar ve diğer hastane personeli

- Antifungal ilaçları uygun reçete etmek
- Her antifungal için endikasyon, doz, süreye uymak
- Lokal antifungal direnç paterninin farkında olmak
- Hastane içindeki çalışmalara iştirak etmek
- Her hastayla el hijyeni ve diğer enfeksiyon kontrol önlemlerini uygulamak

CDC, Antifungal Resistance, 18 August 2016

Teşekkürler…