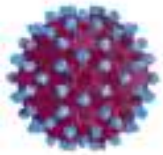
Etkene Yönelik Tedavi; Aspergilloz, Kandidoz, Mukormikoz

Dr. Ziya Kuruüzüm

DEÜTF Enfeksiyon Hastalıkları ve

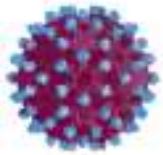
Klinik Mikrobiyoloji AD

Febril Nötropenik Hastada Antifungal Tedavi: Rehberler ve Gerçek Yaşam Verileri, EKMUD, 17.02.2015, Mövenpick Otel, İzmir.

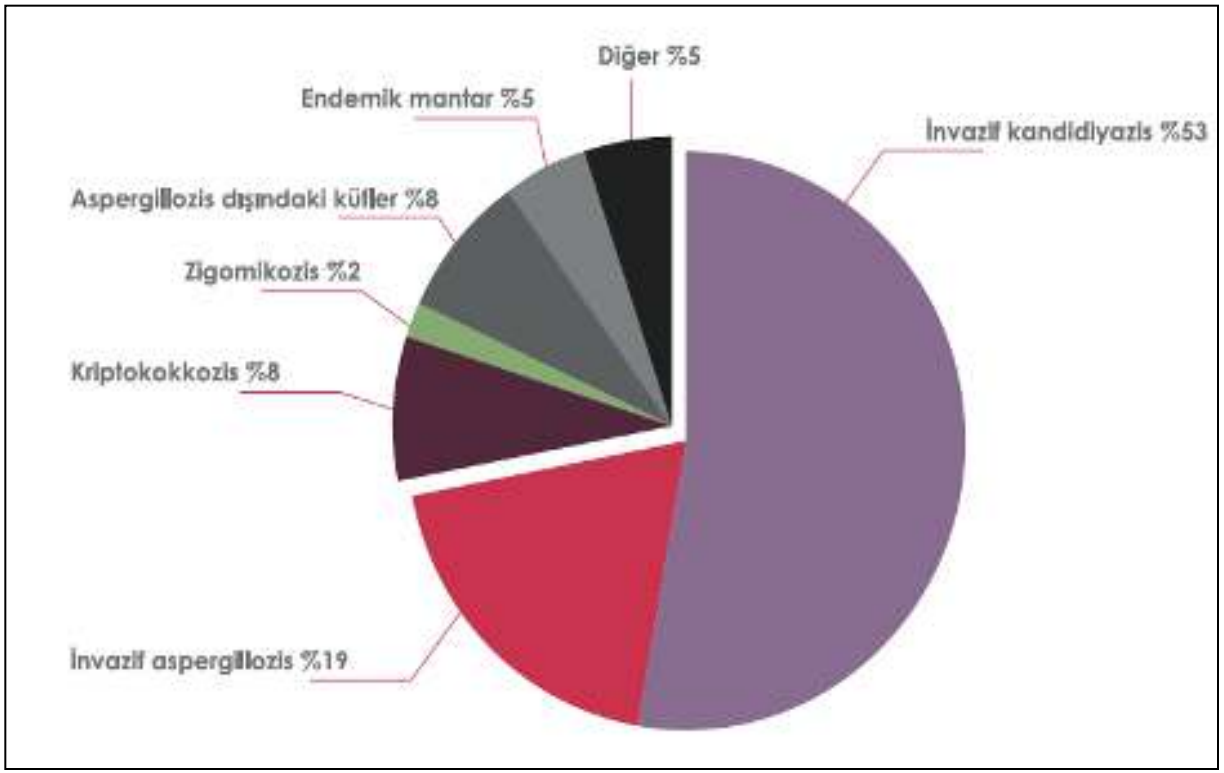


Sunum Planı

- Febril nötropeni ve fungal enfeksiyonlar
- Kandidoz
- Aspergilloz
- Mukormikoz



Fungal enfeksiyonlara en sık yol açan patojenler



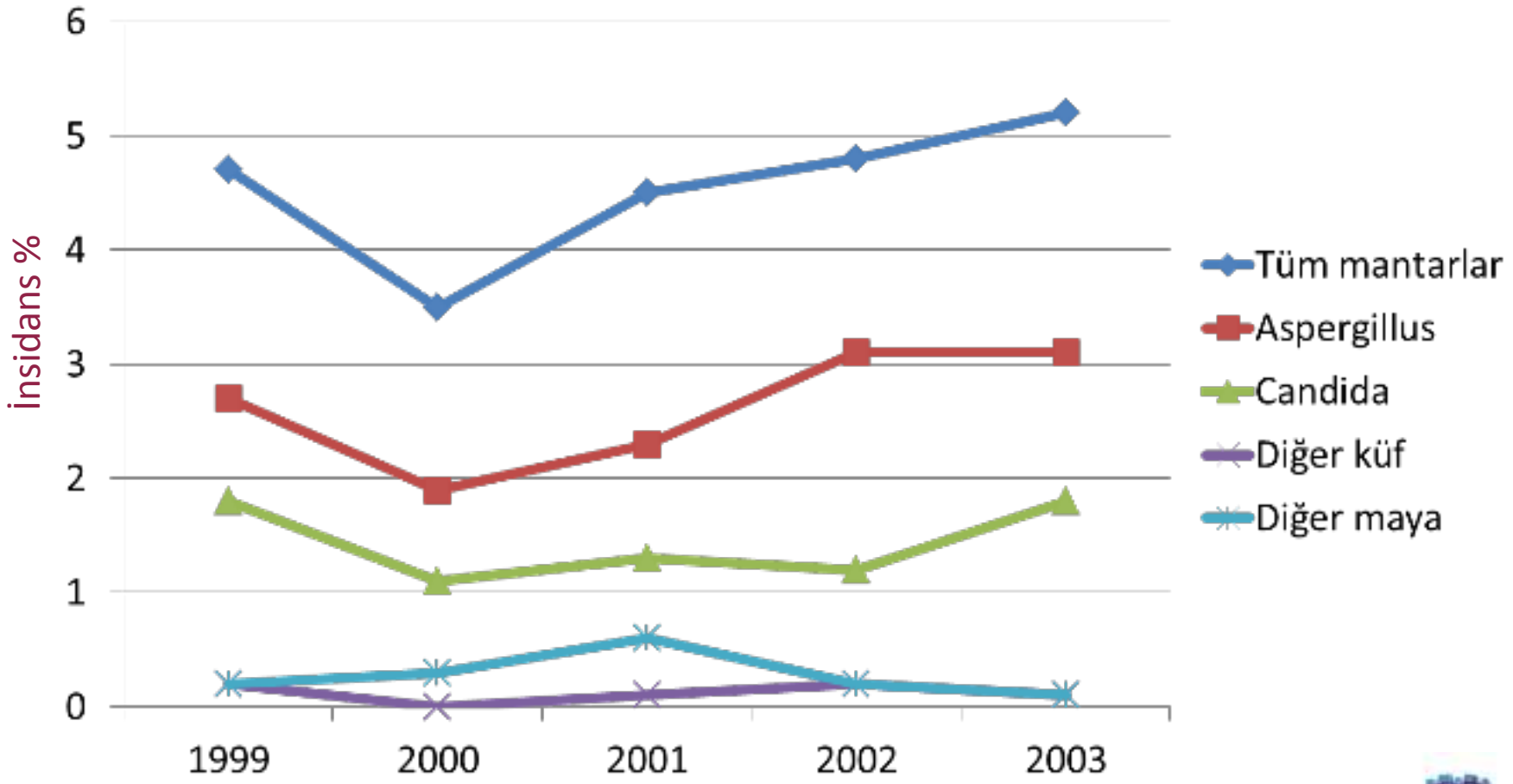
Günümüzde fungal enfeksiyonların %53'ü kandida türleri

Pappas ve ark. 2010'dan uyarlanmıştır.[1]

ABD'deki 15 transplantasyon merkezinden toplanan, 1603 solid organ alıcısından dokümante edilmiş 1208 kanıtlanmış ya da muhtemel İFİ vakasını içeren 12 aylık sağkalım verisi.

Pappas PG et al. Clinical Infectious Diseases 2010; 50:1101–1111.

Hematolojik Maligniteli Hastalarda İFH Epidemiyolojisi



Pagano et al. Haematologica 2006; 91:1068-1075

IFI için Risk Skalası

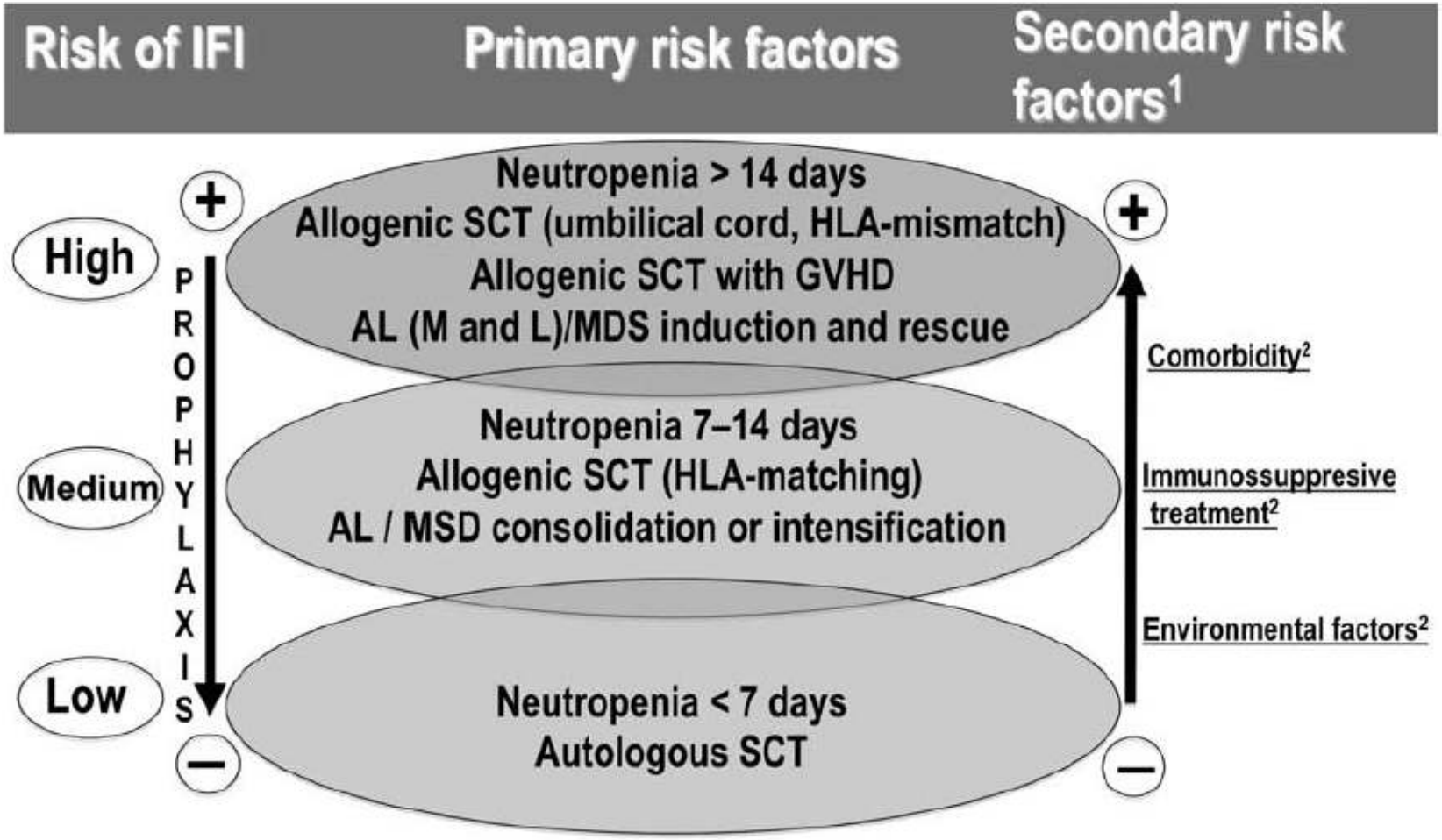
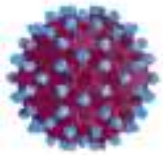


Figure 1 | Classification of the risk groups for IFI.

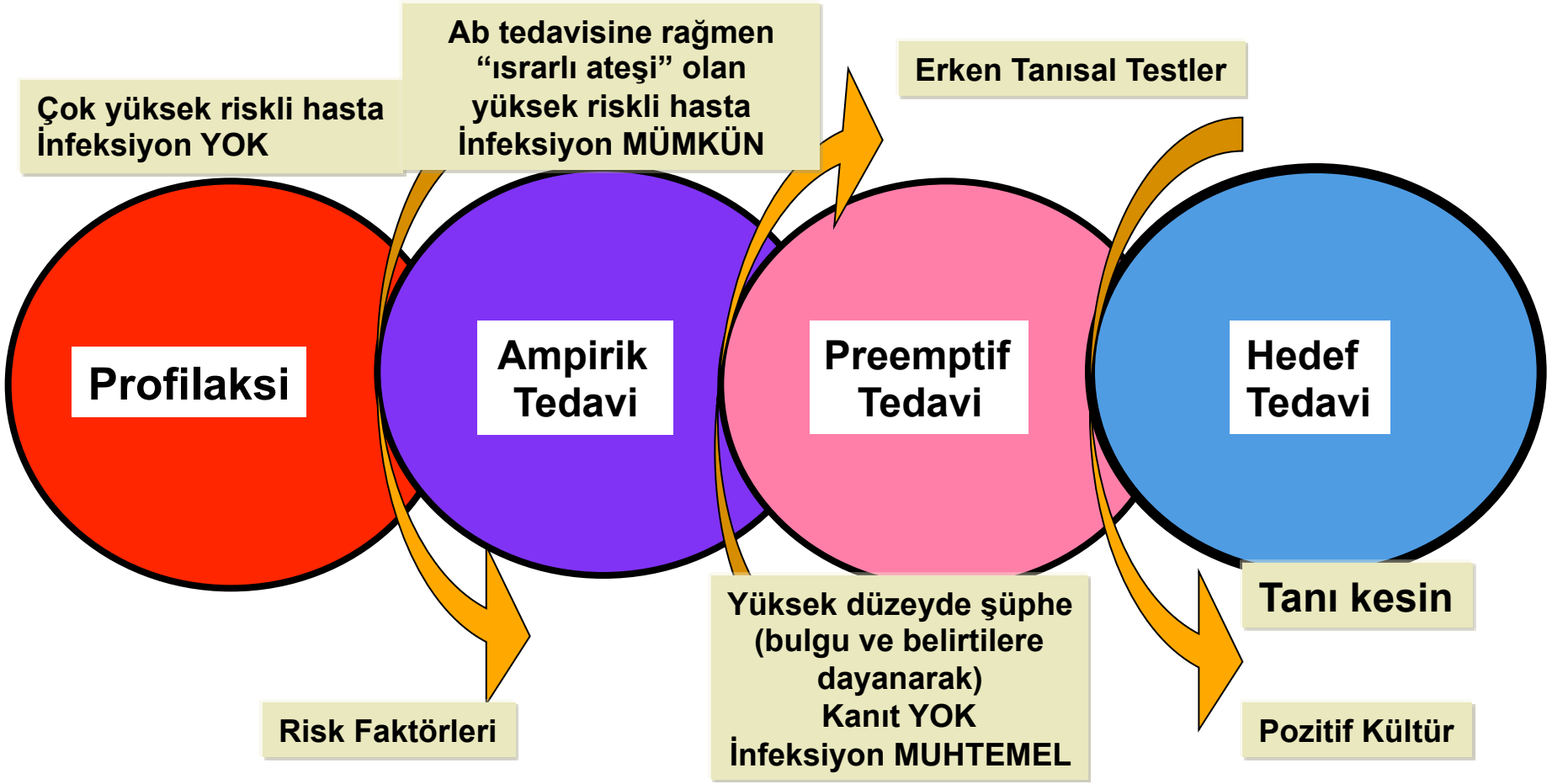
Sekonder risk faktörleri

Ko-morbidite	İmmunsüpresif tedavi	Çevresel faktörler
Yaş > 65 İlerlemiş hastalık Geçirilmiş IFI Demir birikimi Metabolik asidoz Kontrol dışı hiperglisemi CMV infeksiyonu Solunum virusleri ile enfeksiyon KOAH Böbrek yetmezliği Karaciğer yetmezliği Malnütrisyon Genetik polimorfizm (MBL, TLRA-2)	Kortikosteroid Alemtuzumab Yüksek doz citarabine Anti-TNF ajanlar Yüksek doz tüm vücut irradiasyonu	İnşaat HEPA filtresiz odalar

Vallejo et al. 2013

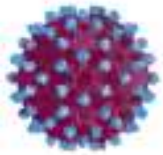


Antifungal Tedavi Yaklaşımları



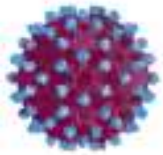
Kandidoz

- İnsanlardaki invazif fungal infeksiyonların en sık nedeni
- Mukokütanöz infeksiyonlardan organ tutulumuna dek değişik ciddiyette tablolar
- Yaşamı tehdit edici



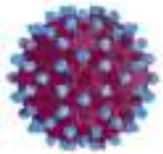
Kandidoz

- Nosokomiyal kan dolaşımı enfeksiyonları üst sıralarda
- Mortaliteye katkısı yetişkinlerde; %15-25 ve çocuklarda %10-15



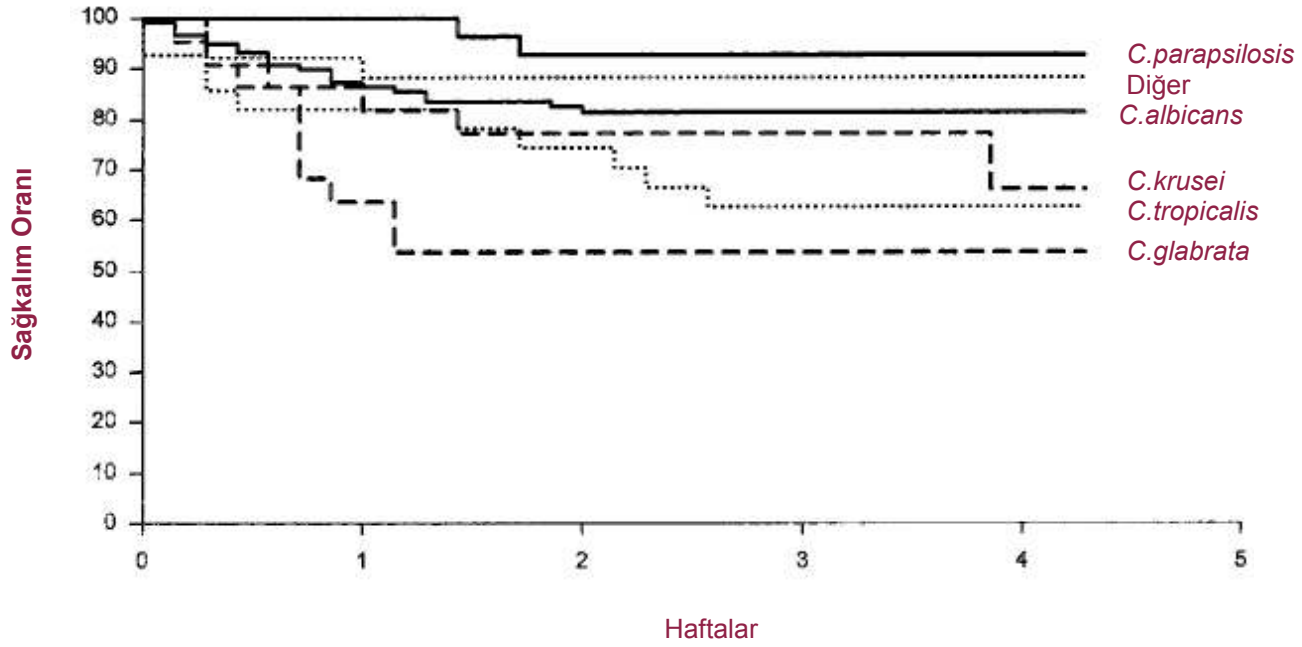
Kandidoz - Risk faktörleri

- Geniş spektrumlu antibiyotik kullanımı
- Santral venöz kateter
- Parenteral nütrisyon
- Renal replasman tedavisi (YB)
- Nötropeni
- İmplante protezler
- İmmünsüpresif tedavi
  - Kortikosteroid
  - Kemoterapi
  - İmmun modülatör



İmmünkompromize hastalarda kandidemiye bağlı mortalite

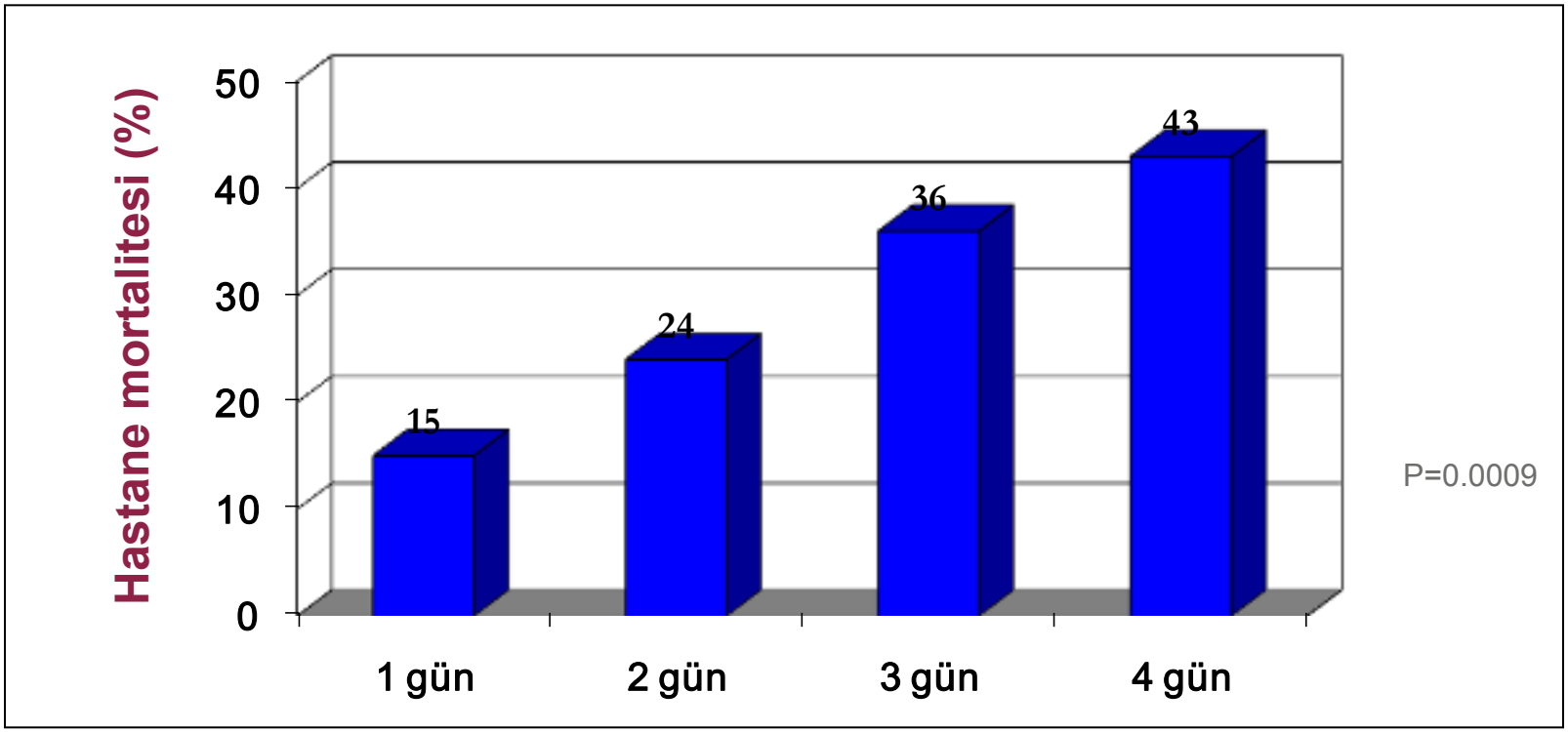
ABD'deki 15 transplantasyon merkezinden toplanan, 1603 solid organ alıcısından elde edilmiş 1208 kanıtlanmış ya da muhtemel İFİ vakasını içeren 12 aylık sağkalım verisi



1.Pappas PG et al. Clinical Infectious Diseases 2010; 50:1101–1111.
2.Viscoli C et al. Clinical Infectious Diseases. 1999; 28:1071-9.
3.Hof H. Mycoses. 2008;51 Suppl 1:1-6.
4.Cornely OA et al. Mycoses. 2010 Oct 11. doi: 10.1111/j.1439-0507.2010.01947.x.
5.Chamilos G et al. Clin Infect Dis. 2008;47:503-9.

Kandidemi tedavisinde gecikme ve mortalite

Antifungal tedavi başlama zamanı ile mortalite arasındaki ilişki

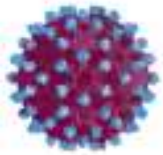


Antifungal tedavi başlamada gecikme (gün)

1.Garey KW et al. CID 2006; 43: 25-31.
2.Morrell et al. AAC 2005; 49: 3640-3645.

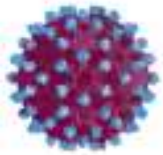
Kandidoz tedavisi ve anti fungal ajanlar

- Polyenler
  - AmB-d, L-AmB, AmB lipid kompleks,
- Triazoller
  - Flukonazol, itrakonazol, vorikonazol, posakonazol
- Ekinokandinler
  - Kaspofungin, anidulafungin, micafungin
- Flusitozine



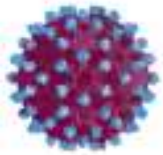
Nötropeni ve Kandidemi

- Nötropenik hastalarda yaşamı tehdit edici
  - Aku dissemine kandidiyazis
  - Sepsis benzeri tablo
  - Multi organ yetmezliği
  - Ölüm
- *Candida tropicalis* özellikle virulan



Nötropeni ve Kandidemi

- Yeterli randomize kontrollu çalışma yok
- Veriler, tek kollu ya da çoğunluğu non-nötropenik olguları kapsayan çalışmalardan



COMPARISON OF CASPOFUNGIN AND AMPHOTERICIN B FOR INVASIVE CANDIDIASIS

JORGE MORA-DUARTE, M.D., ROBERT BETTS, M.D., COLEMAN ROTSTEIN, M.D., ARNALDO LOPES COLOMBO, M.D., LUIS THOMPSON-MOYA, M.D., JUANITA SMIETANA, B.S., ROBERT LUPINACCI, M.S., CAROLE SABLE, M.D., NICHOLAS KARTSONIS, M.D., AND JOHN PERFECT, M.D., FOR THE CASPOFUNGIN INVASIVE CANDIDIASIS STUDY GROUP*

CHARACTERISTIC	CASPOFUNGIN (N=109)	AMPHOTERICIN B (N=115)
Sex — no. (%)		
Male	56 (51.4)	69 (60.0)
Female	53 (48.6)	46 (40.0)
Age — yr		
Median	56	55
Range	17–84	18–81
APACHE II score		
≤20 — no. (%)	88 (80.7)	92 (80.0)
>20 — no. (%)	21 (19.3)	23 (20.0)
Mean score	14.8	15.4
Neutropenia — no. (%)†		
Yes	14 (12.8)	10 (8.7)
No	95 (87.2)	105 (91.3)

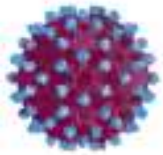


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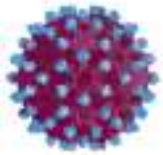
TABLE 4. FAVORABLE RESPONSES TO TREATMENT.

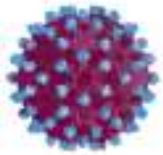
TIME POINT	MODIFIED INTENTION-TO-TREAT ANALYSIS		PATIENTS WHO MET CRITERIA FOR EVALUATION	
	CASPOFUNGIN (N=109)	AMPHOTERICIN B (N=115)	CASPOFUNGIN (N=88)	AMPHOTERICIN B (N=97)
	no. with a favorable response/total no. (%)			
End of intravenous therapy	80/109 (73.4)	71/115 (61.7)	71/88 (80.7)	63/97 (64.9)*
Absolute neutrophil count at enrollment				
<500/mm³	7/14 (50.0)	4/10 (40.0)	6/8 (75.0)	3/8 (37.5)
≥500/mm³	73/95 (76.8)	67/105 (63.8)	65/80 (81.2)	60/89 (67.4)



Kandidemi tedavisinde Mikafungin vs L-AmB

- Kandidemi ve invazif kandidiyazisli 531 olgu
- Faz III, non-inferiorite çalışması
- Değerlendirmeye alınan
  - Mikafungin grubunda 202 hasta, başarı: 181 (%89,6)
  - L-AmB grubunda 190 hasta, başarı: 170 (%89,5)
  - Nötropenik olan; %68 - %61

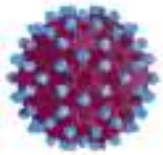
Lancet. 2007 May 5;369(9572):1519-27.



Micafungin versus Caspofungin for Treatment of Candidemia and Other Forms of Invasive Candidiasis

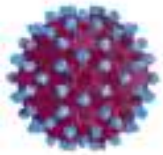
Peter G. Pappas,[1] Coleman M. F. Rotstein,[9] Robert F. Betts,[2] Marcio Nucci,[10] Deepak Talwar,[11] Jan J. De Waele,[13] Jose A. Vazquez,[3] Bertrand F. Dupont,[14] David L. Horn,[4] Luis Ostrosky-Zeichner,[6] Annette C. Reboli,[7] Byungse Suh,[5] Raghunadharao Digumarti,[12] Chunzhang Wu,[8] Laura L. Kovanda,[8] Leah J. Arnold,[8] and Donald N. Buell[8]

- 595 hasta, (kandidemi %85)
- 191 hasta mikafungin 100 mg/gün, 22 (%11,5)
- 199 hasta mikafungin 150 mg/gün, 17 (%8,5)
- 188 hasta caspofungin standart doz, 11 (%5,9)



Tedavi başarısı

- Mikafungin 100 mg/gün: %76,4. Nötropenik (18/22) %81,8
- Mikafungin 150 mg/gün: %71,4. Nötropenik (9/17) %52,9
- Kaspofungin: %72,3. Nötropenik (7/11) %63,6



Efficacy of Caspofungin against Invasive *Candida* or Invasive *Aspergillus* Infections in Neutropenic Patients

- 27 invazif kandidiyazisli nötropenik hasta
- Kaspofungin monoterapisi
- Standart doz

- Tedavi başarısı; %63 (17/27)

Cancer 2006; 106:466–73.

IDSA Önerileri

	IDSA			
	İnvazif aspergillozis şüphesi için ampirik tedavi	Doğrulanmış invazif pulmoner aspergillozisin primer tedavisi	Nötropenik hastalarda invazif kandidiyazis şüphesi için ampirik tedavi	Nötropenik hastalarda doğrulanmış invazif kandidiyazisin tedavisi
L- amfoterisin b	AI	AI (alternatif)	AI	AII
Kaspofungin	AI	BII**	AI	AII
Vorikonazol	AI	AI	BI	BIII

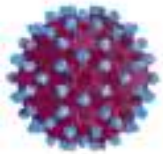


Table 3 | Factors to be considered when selecting an antifungal agent for empirical treatment

Epidemiology of invasive fungal infection (IFI)	*Candida* *Aspergillus* Other filamentous fungi		
Spectrum of the antifungal	***Candida***	***Aspergillus***	**Other filamentous fungi**
Amphotericin B	+++	+++	+++
Voriconazole	+++	+++	++
Caspofungin	+++	+++	-
Type of activity	**Yeasts**		**Filamentous fungi**
Amphotericin B	Fungicidal		Fungicidal
Voriconazole	Fungistatic		Fungicidal
Caspofungin	Fungicidal		Fungistatic
Clinical experience	**Efficacy against *Aspergillus***		**Breakthrough aspergillosis and mucormycosis**
Amphotericin B	+ + +		-
Voriconazole	+ + +		+
Caspofungin	+ +		+
Severity of infection	For empirical treatment select the antifungal agent with the highest efficacy and the broadest spectrum of action		
Prophylaxis with triazole or candin	In case of suspected IFI begin with liposomal amphotericin B		

Antifungal Ajanların Etki Spektrumu

	Vorikonazol	Amfoterisin B*	Kaspofungin
Aspergillus spp.			
A. fumigatus			
A. flavus			
A. niger			
A. terreus			
Candida spp.			
C. albicans			
C. glabrata			
C. krusei			
C. lusitaniae			
C. parapsilosis			
C. tropicalis			
Cryptococcus neoformans			
Fusarium spp.			
Scedosporium aspiospermum			
Scedosporium prolificans			
Zygomycetes			

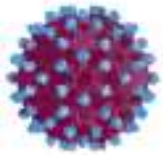
DUYARLI
DİRENÇLİ
DEĞİŞKEN

* Lipid formülasyonlar dahil

Verweij PE ve ark. Drug Res Updates 2009;141–7
Pfaller MA ve ark. J Clin Microbiol 2010;48:1366–77
Dodds Ashley ES ve ark. Clin Infect Dis 2006;43:S28–39

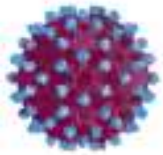
Kandidoz Tedavisi - Sonuç

- Sınırlı veri
- Nötropenik/non-nötropenik veriler farklı değil
- Flukonazol ya da vorikonazol daha az başarılı değil
- Çoğu klinisyenin tercihi caspofungin ya da L-AmB (fungisidal)
- Tedavi süresi 14 gün (negatif kan kültüründen sonra)
- Kateter çıkarılması çoğunlukla gerekli



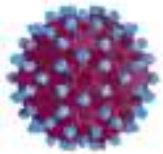
Aspergilloz

- Aspergillus türleri immun kompromize hastalarda önemli morbidite ve mortalite nedeni
- İnvazif Aspergilloz (İA), hematolojik kök hücre nakil hastalarındaki akciğer kökenli en mortal enfeksiyonlardır.



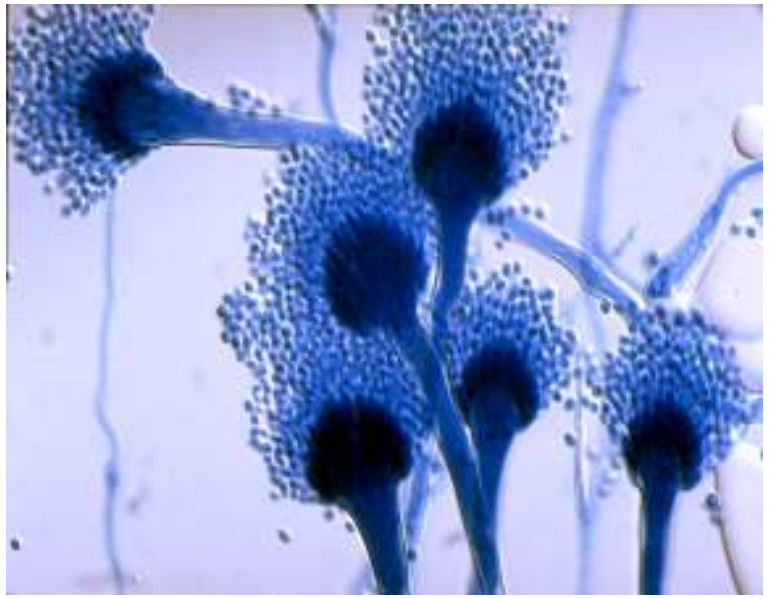
Aspergilloz

- Aspergillus türleri aynı zamanda;
- Kronik
- Saprofitik
- Allerjik
  - ABPA, allerjik sinüzit vb.



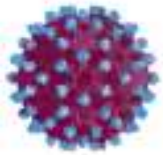
Aspergillus türleri

- *Aspergillus fumigatus* (en sık)
- *Aspergillus* flavus (ikinci en sık)
- *Aspergillus niger*
- *Aspergillus terreus*



Aspergilloz tedavisi ve anti-fungal ajanlar

- Polyenler
  - AmB-d, L-AmB, AmB lipid kompleks,
- Triazoller
  - İtrakonazol, vorikonazol, posakonazol
- Ekinokandinler
  - Kaspofungin



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Amphotericin B	+ + +		-
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Caspofungin	+ +		+
Severity of infection	For empirical treatment select the antifungal agent with the highest efficacy and the broadest spectrum of action		
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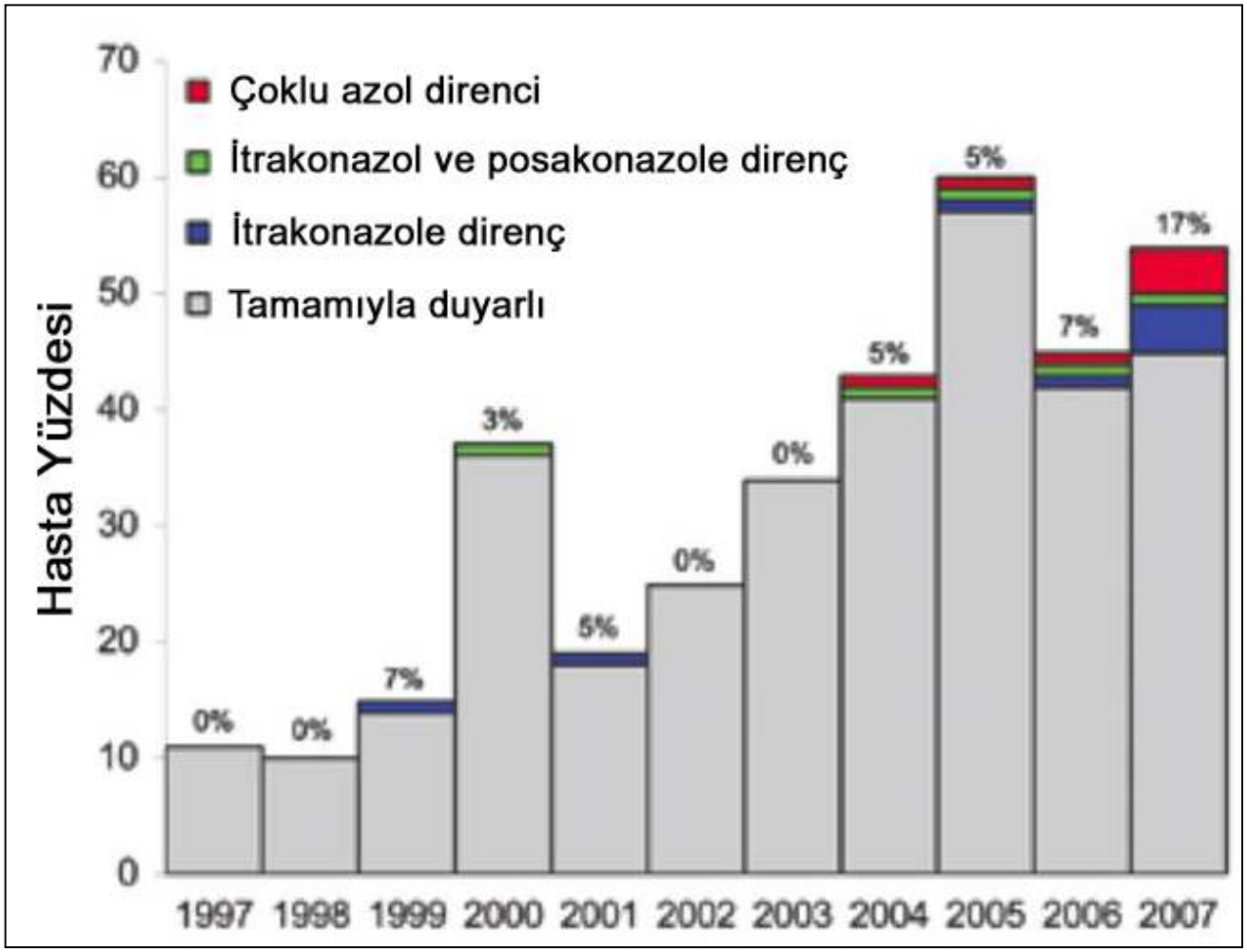
A.fumigatus izolatlarında azol direnci

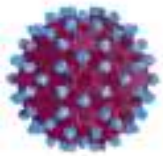


Howard SJ et al. Emerg Infect Dis 2009;15:1068.

Aspergillus Türlerinde Azol Direnci

- Her geçen gün daha çok rapor edilmeye başlandı.
- Manchester, tek merkez: %15
  - Uzun süre azol antifungal maruziyeti
- Hollanda: ülke genelinde % 5.3, Nijmegen %10
  - Tarımda azol kullanımı: TR/L98H mutasyonu
- Özellikle *A.fumigatus*
- Polyen ve ekinokandinler için çok nadir

Verweij et al.2009; Mayr & Lass-Florl 2011



İnvazif aspergilloz tedavisinde Vorikonazol vs Amfoterisin B dezoksikolat

The New England Journal of Medicine

VORICONAZOLE VERSUS AMPHOTERICIN B FOR PRIMARY THERAPY OF INVASIVE ASPERGILLOSIS

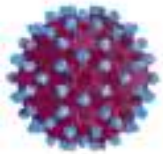
RAOUL HERBRECHT, M.D., DAVID W. DENNING, F.R.C.P., THOMAS F. PATTERSON, M.D., JOHN E. BENNETT, M.D., REGINALD E. GREENE, M.D., JÖRG-W. OESTMANN, M.D., WINFRIED V. KERN, M.D., KIEREN A. MARR, M.D., PATRICIA RIBAUD, M.D., OLIVIER LORTHOLARY, M.D., PH.D., RICHARD SYLVESTER, SC.D., ROBERT H. RUBIN, M.D., JOHN R. WINGARD, M.D., PAUL STARK, M.D., CHRISTINE DURAND, M.D., DENIS CAILLOT, M.D., ECKHARD THIEL, M.D., PRANATHARTHI H. CHANDRASEKAR, M.D., MICHAEL R. HODGES, M.D., HARAN T. SCHLAMM, M.D., PETER F. TROKE, PH.D., AND BEN DE PAUW, M.D., FOR THE INVASIVE FUNGAL INFECTIONS GROUP OF THE EUROPEAN ORGANISATION FOR RESEARCH AND TREATMENT OF CANCER AND THE GLOBAL ASPERGILLUS STUDY GROUP*

İnvazif aspergilloz tedavisinde Vorikonazol vs Amfoterisin B dezoksikolat

- **Herbrecht et al.**
- **Randomize, açık etiketli, 12 haftalık çalışma**
- **Hematolojik malignensili veya HSCT uygulanmış hastalar**
- **277 IA vakası (kesin veya olası)**
- **IV Vorikonazol ile IV amfoterisin B deoksikolat karşılaştırması**
  - **Voriconazol (144 hasta): 1. gün 2 doz 6 mg/kg, ardından yedi gün günde 2 kez 4 mg/kg, ardından günde 2 kez oral 200 mg**
  - **AmB-d (133 hasta): 1-1,5 mg/kg/gün**
  - **Her iki grupta da hastaların % 45'i nötropenik**

Sonuç

- Genel başarı oranı
  - Vorikonazol: %52,8
  - AmB-d: %31,6
- Sağkalım oranı
  - Vorikonazol: %70,8
  - AmB-d: %57,9
- Vorikonazol, bu çalışma ile kılavuzlardaki yerini aldı

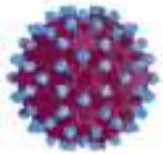


Ambiload Çalışması

MAJOR ARTICLE

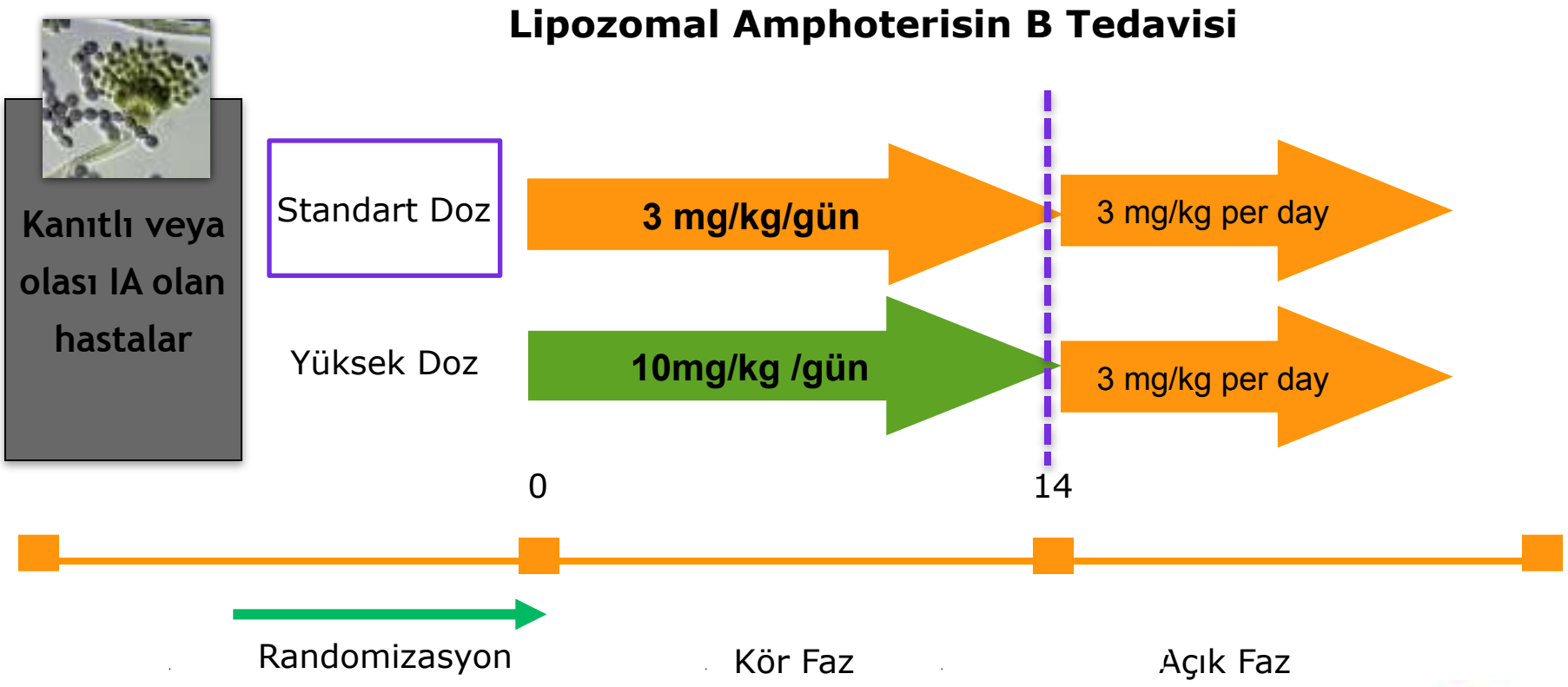
Liposomal Amphotericin B as Initial Therapy for Invasive Mold Infection: A Randomized Trial Comparing a High–Loading Dose Regimen with Standard Dosing (AmBiLoad Trial)

Oliver A. Cornely, Johan Maertens, Mark Bresnik, Ramin Ebrahimi, Andrew J. Ullmann, Emilio Bouza, Claus Peter Heussel, Olivier Lortholary, Christina Rieger, Angelika Boehme, Mickael Aoun, Heinz-August Horst, Anne Thiebaut, Markus Ruhnke, Dietmar Reichert, Nicola Vianelli, Stefan W. Krause, Eduardo Olavarria, and Raoul Herbrecht, for the AmBiLoad Trial Study Group*



AmBiLoad – Çalışma Tasarımı

Amaç, IA tedavisinde standart doz yerine yüksek doz tedavinin daha etkili olup olmadığını araştırmak



Cornely et al. Clinical Infectious Diseases 2007; 44:1289–97

Herbrecht ve AmBiLoad Çalışmaları Karşılaştırma

	Herbrecht 2002 (vorikonazol)	AmBiload 2007 (LAMB 3mg)
Çalışma Tasarımı	Randomize, kör olmayan, açık etiketli	Randomize, prospektif, çift-kör
Hasta Sayısı	277	201
İlaç Dozu	Vorikonazol = 1.gün, i.v. 6 mg/kg 2x1 yükleme sonra en az 7 gün boyunca i.v. 4 mg/kg 2x1, Amfoterisin B = 1-1.5 mg/kg/gün	Yüksek doz (10 mg/kg/gün) AmBisome® 14. gününden sonra 3 mg/kg Am) Standart d n) AmBisom
Hasta Özellikleri	>12 yaş, Allo/Otolog KİT, hematolojik kanser , aplas veya AIDS, steroid tedavi kullanımı veya SOT veya immünkom kanıtlı/olası invazif aspergillozis tanısı almış hastalar.	
Ortalama Yaş	48.5	
Cinsiyet (E/K)	68/32	
Ortalama ağırlık (kg)	70.4	68.3
Hem. Malinite (%)	52	93
Başlangıçta Nötropeni (%)	45	71

Daha Yüksek Riskli Hastalar

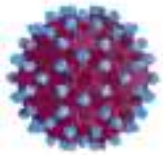
Herbrecht ile karşılaştırma

	Herbrecht 2002		AmBiload 2007	
12.haftada Tedavi Başarısı (tam veya kısmi)	Vorikonazol:	% 53	3 mg LAMB	%50
	Amfoterisin B:	% 32	10 mg LAMB	%46
12.Haftada Sağkalım	Vorikonazol:	% 71	3 mg LAMB	%72
	Amfoterisin B:	% 58	10 mg LAMB	%59

Amphotericin B Lipid Complex Versus Liposomal Amphotericin B Monotherapy for Invasive Aspergillosis in Patients With Hematologic Malignancy

- 381 kanıtlanmış veya yüksek olasılıklı IA'lı hasta
- Retrospektif
- 52 AmB lipid kompleks, 29 (%55,8) nötropenik
- 106 L-AmB, 52 (%49,1) nötropenik
- Genel başarı çok düşük (%8)
- İlerlemiş ciddi olgular

Cancer 2008;112: 1282–1287.

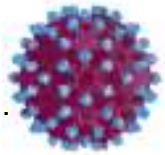


An EORTC Phase II study of caspofungin as first-line therapy of invasive aspergillosis in haematological patients

C. Viscoli[1]*, R. Herbrecht[2], H. Akan[3], L. Baila[4], A. Sonet[5], A. Gallamini[6], A. Giagounidis[7], O. Marchetti[8], R. Martino[9], L. Meert[4], M. Paesmans[10], L. Ameye[10], M. Shivaprakash[11], A. J. Ullmann[12] and J. Maertens[13] on behalf of the Infectious Disease Group of the EORTC†

[1]San Martino University Hospital, Genova, Italy; [2]University Hospital, Strasbourg, France; [3]Ankara University School of Medicine, Ankara, Turkey; [4]EORTC, Brussels, Belgium; [5]Cliniques Universitaires De Mont Godinne, Yvoir, Belgium; [6]Ospedale Santa Croce, Cuneo, Italy; [7]St Johannes Hospital Medizinische Klinik II, Duisburg, Germany; [8]Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland; [9]University Hospital, Barcelona, Spain; [10]Institut Jules Bordet, Brussels, Belgium; [11]Merck & Co., Inc., Whitehouse Station, NJ, USA; [12]3rd Medical Department, Johannes Gutenberg University, Mainz, Germany; [13]UZ Gasthuisberg, Leuven, Belgium

- Hematolojik kanserli ve OKİT yapılan
- İlk tedavi olarak kaspofungin, standart doz
- Toplam 61 olgu (%98 probable)
- 51 olgu (%85) nötropenik
- Tam ve kısmi yanıt; 20/61 (%33) (hipotezin altında)



J Antimicrob Chemother 2009; 64: 1274–1281.

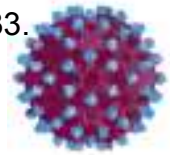
ORIGINAL ARTICLE

Caspofungin first-line therapy for invasive aspergillosis in allogeneic hematopoietic stem cell transplant patients: an European Organisation for Research and Treatment of Cancer study

R Herbrecht[1], J Maertens[2], L Baila[3], M Aoun[4], W Heinz[5], R Martino[6], S Schwartz[7], AJ Ullmann[8], L Meert[3], M Paesmans[3], O Marchetti[9], H Akan[10], L Ameye[4], M Shivaprakash[11] and C Viscoli[12], for the Infectious Diseases Group of the EORTC

- Hematolojik kanserli ve AKİT yapılan
- İlk tedavi olarak kaspofungin, standart doz
- Toplam 24 olgu
- 12 olgu (%50) nötropenik
- Tam ve kısmi yanıt; 10/24 (%42)
- Çalışma erken sonlandırılmış

Bone Marrow Transplant 2010,45:1227-33.



Kılavuz Önerileri

	ECIL-3 VE 4		
	İnvazif pulmoner aspergillozisin tedavisi	Doğrulanmış invazif kandidiyazisin tedavisi***	Nötropenik hastalarda İFİ şüphesi için ampirik tedavi
L- Amfoterisin	BI	AI	AI
Kaspofungin	CII	AI	AI§
Vorikonazol	AI	AI††	BI§§

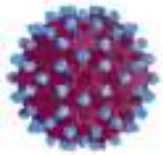
1.Herbrecht et al. 2011 ECIL-4 guideline slides. Antifungal therapy in leukemia patients. www.eortc.org/home/IDG/ECIL.html
2.Marchetti et al. 2009 ECIL-3 guideline slides. Empirical Antifungal therapy. www.eortc.org/home/IDG/ECIL.html

Kılavuz Önerileri

	IDSA			
	İnvazif aspergillozis şüphesi için ampirik tedavi	Doğrulanmış invazif pulmoner aspergillozisin primer tedavisi	Nötropenik hastalarda invazif kandidiyazis şüphesi için ampirik tedavi	Nötropenik hastalarda doğrulanmış invazif kandidiyazisin tedavisi
L- Amfoterisin	AI	AI (alternatif)	AI	AII
Kaspofungin	AI	BII**	AI	AII
Vorikonazol	AI	AI	BI	BIII

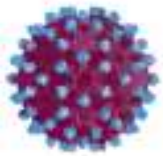
Mukormikoz

- Hematolojik maligniteli ve AKİT hastaları
- Gittikçe artan bir insidans
- Otopsi serilerinde %0,4-0,9
- AML %1-1,9
- Yaşamı tehdit edici



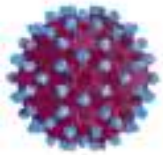
Mukormikoz insidansı

Reference	Years	Population	Cases	%
Conventional therapy				
Pagano *et al.*[8]	1987-1995	3148 acute leukemia	37	1
Nosari *et al.*[9]	1987-1999	653 acute leukemia	13	1.6
Kontoyiannis *et al.*[10]	1989-1998 1989–1993 1994–1998	624 autopsy in HMs 88207 cancer patients 82490 cancer patients	12 7 17	1.9 0.008 0.02
Pagano *et al.*[12]	1999-2003	11802 HM	14	0.1
HSCT				
Marr *et al.*[13]	1985-1999	5589 HSCT	29	0.5
Kontoyiannis *et al.*[15]	2001-2006	16200 HSCT	77	0.4
Pagano *et al.*[12]	1999-2003	1249 alloHSCT 1979 autoHSCT	1 0	0.08
Garcia Vidal *et al.*[14]	1998-2002	1248 HSCT	8	0.6
Neofytos *et al.*[1]	2004-2007	alloHSCT autoHSCT	12 8	
Xhaard *et al.*[16]	2003-2008	4138 alloHSCT	23	0.56



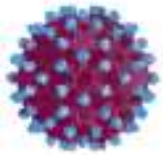
Mikrobiyoloji

- *Rhizopus spp. (en sık)*
- *Mucor spp.*
- *Rhizomucor spp.*
- *Lichtheimia (Absidia)*



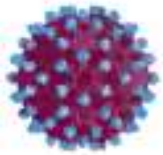
En sık tutulan organlar

- *Akciğerler (en sık)*
- *Paranazal sinüsler*
- *Beyin*
- *Deri*
- *Dissemine enfeksiyonlar*



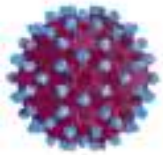
Aspergilloz – Mukor ayrımında ipuçları

- Klinik ve radyolojik görünüm aynı
- Önceden ya da devam eden vorikonazol profilaksisi
- Paranazal sinüs tutulumu
- DM
- On taneden fazla pulmoner nodül
- Plevral effüzyon



Tanı

- Hızlı tanı yaşamsaldır, tedavi acil olarak başlanmalıdır
- Kan testi yok
- Doku örneği alınmalı
  - Histopatoloji
  - Kültür
- Septasız, geniş çaplı (5-25 μ) ve 90° dallanan hifler



Antifungal Ajanların Etki Spektrumu

	Vorikonazol	Amfoterisin B*	Kaspofungin
Aspergillus spp.			
A. fumigatus			
A. flavus			
A. niger			
A. terreus			
Candida spp.			
C. albicans			
C. glabrata			
C. krusei			
C. lusitaniae			
C. parapsilosis			
C. tropicalis			
Cryptococcus neoformans			
Fusarium spp.			
Scedosporium aspiospermum			
Scedosporium prolificans			
Zygomycetes			

DUYARLI
DİRENÇLİ
DEĞİŞKEN

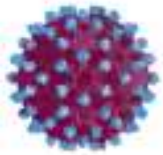
* Lipid formülasyonlar dahil

Verweij PE ve ark. Drug Res Updates 2009;141–7
Pfaller MA ve ark. J Clin Microbiol 2010;48:1366–77
Dodds Ashley ES ve ark. Clin Infect Dis 2006;43:S28–39

Bazı anti-fungallerin MIC değerleri (ECIL-3)

Table 5. Comparative activity of amphotericin B, posaconazole and itraconazole against 216 clinical isolates of 10 Mucorales.

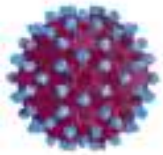
	Amphotericin B % with MIC ≤1 μg/mL	Posaconazole % with MIC ≤0.5 μg/mL	Itraconazole % with MIC ≤0.5 μg/mL
Rhizopus sp (101)	100	80	62
Rhizopus arrhizus (20)	100	64	50
Rhizopus microsporus (12)	100	78	60
Mucor sp. (41)	94	70	57
Mucor circinelloides (6)	100	0	0
Rhizomucor sp.(5)	100	67	67
Lichtheimia sp. (3)	100	100	50
Lichtheimia corymbifera (9)	100	100	100
Cunninghamella sp. (13)	63	75	29
Apophysomyces elegans (6)	100	83	80



Mukormikozda tedavi önerileri-1 (ECİL-3)

Table 3. ECIL-3 recommendations for first-line treatment of mucormycosis.

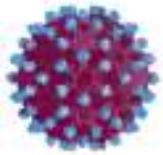
Management should include antifungal therapy, control of underlying conditions and surgery	AII
Antifungal therapy	
AmB deoxycholate[4,29,30]	CII
Liposomal AmB[16,29-34], 5-10 mg/kg[35,36]	BII[1]
ABLC[37,29], 5-7.5 mg/kg[35]	BII1
ABCD[42,45]	CII
Posaconazole[16,17] 400 mg bid	CIII[2]
Combination therapy[39]	CIII
Control of underlying condition[5,42,43]	AII[3]
Surgery	
-rhino-orbito-cerebral[44-47]	AII
-soft tissue[48,49]	AII
-localized pulmonary lesion[50,51]	BII
-disseminated[22]	CIII[4]
Hyperbaric oxygen	CIII



Mukormikozda tedavi önerileri-2 (ECİL-3)

Table 4. ECIL-3 recommendations for second-line and maintenance treatment of mucormycosis.

Second-line treatment: first-line treatment intolerance or failure[1]	
Posaconazole 400 mg bid[52,53]	BII
Combination lipid AmB and caspofungin[39]	BII
Combination lipid AmB and posaconazole	CIII
Combination with deferasirox NOT recommended[104]	AI
Maintenance therapy Posaconazole	BIII[2]




Sabrınız için teşekkürler