FEN YÖNETİMİ:ÇÖZÜM BEKLEYEN SORUNLAR

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Enfeksiyon Hastalıkları ve Klinik Bakteriyoloji Anabilim Dalı


TEDAVİDE YOL HARİTASI

Zaman kaybedilmemeli…


Erken tanı
Erken tedavi
İmmun Fonksiyonların düzelmesi


sunday CHINA DAILY
LOVE THAT OKTOBERFEST!
MAYAN QUEEN IMAGES OF TIMELESS BEAUTY, P6
SUPER BUGS
The next time you pop an antibiotic, consider this: You may be helping a dormant virus mutate into an even more lethal killer. Mike Peters tells you how.

ERKEN VE DOĞRU TANI HENÜZ BAŞARILAMAMIŞ BİR HEDEF

- CT/GM /ß-Glucan
- Duyarlılık sorunu
- Özgün olmayan göstergeler
- Örneklem için invazif işlemler

MİKROBİYOLOJİK İŞLEMLER

KAN KÜLTÜRÜ :
Volum (20 mL/set)
2 set/epizod

SEPTİFAST
MALDİ-TOF

Reimer LG, et al. Clin Microbiol Rev 1994

Hematojen Kandidiyaziste Kan Kültürleri

Maksymiuk et al. Am J Med 1984;77(Suppl.4D):20

İlk 48 saat → %8

1. hafta → %18

En iyi teknikle≈ % 50- 70

2-3 gün - Tanımlama için

Bazı türler için; *C.glabrata*

<%40

Empirik antibiyotik başlarken…

- Olası etken/etkenler
- Önceden izole edilen etkenler
- Önceki antibiyotik kullanımı
- Etkene özgü yerel direnç/duyarlılık oranları

G.Ü.T.F. VERİLER

- **ESBL (+)**

  2001-2003: E.*coli* %19.9, *Klebsiella* %20,

  2008-2010: *E.coli* %30.5, *Klebsiella* %20

- ***Klebsiella*; %11 karbapenem direnci**
- **İlk kez 2009 - 2 suş karbapenm direnci**
- **OXA-48 (+), TEM, CTX-M (-), IMP, VIM ve KPC (-)**

Türkiye'de ilk NDM

LETTER TO THE EDITOR

NDM-1-Producing *Klebsiella pneumoniae* Now in Turkey

- Irak'tan gelen bir hasta
- Kan kültüründe üreme

Antimicrob Agents Chemother. 2012 May; 56(5): 2784–2785.

Article published online: 27 March 2014
New Microbe New Infect 2014; **2:** 50–51

LETTER TO THE EDITOR 10.1002/nmi2.42

KPC-producing *Klebsiella pneumoniae*, finally targeting Turkey

J. Labarca[1,2], L. Poirel[1,3], M. Özdamar[4], S. Turkoglü[4], E. Hakko[5] and P. Nordmann[1,3]

1) *INSERM U914 "Emerging Resistance to Antibiotics", K.-Bicêtre, France,* 2) *Departamento de Medicina Interna, Hospital Clínico Pontificia Universidad Católica de Chile, Santiago, Chile,* 3) *Medical and Molecular Microbiology Unit, Department of Medicine, Faculty of Science, University of Fribourg, Switzerland,* 4) *Department of Microbiology and* 5) *Department of Infectious Diseases, Anadolu Medical Centre, Kocaeli, Turkey*

Abstract

We report here the first identification of the worldwide spread of *Klebsiella pneumoniae* carbapenemase-2-producing and carbapenem-resistant *K. pneumoniae* clone ST258 in Turkey, a country where the distantly-related carbapenemase OXA-48 is known to be endemic. Worryingly, this isolate was also resistant to colistin, now considered to be the last-resort antibiotic for carbapenem-resistant isolates.

baumannii, and a rectal swab taken for screening purposes grew an extended-spectrum β-lactamase-producing *K. pneumoniae*. The patient was treated with meropenem for 14 days and a carbapenem-resistant *K. pneumoniae* (isolate A) was isolated from an endotracheal aspirate culture 21 days after her admission. Colistin was added to the meropenem and, after 10 days, endotracheal aspirate cultures remained negative and the antibiotic regimen was discontinued. Four days after the antibiotherapy was stopped, a carbapenem-resistant and colistin-resistant *K. pneumoniae* (isolate B) was recovered from an endotracheal aspirate culture. The patient developed sepsis, multiple organ failure and died at day 56 of her hospitalization.

Susceptibility testing performed and interpreted according to the updated CLSI guidelines [2] showed that *K. pneumoniae* isolates A and B were susceptible only to cefepime, but were resistant to all other β-lactams including carbapenems. The MICs of carbapenems for both isolates determined by E-test (bioMérieux, La Balme-les-Grottes, France) were 8, 8, and 32 mg/L for imipenem, meropenem and ertapenem, respectively. In addition, they were resistant to all aminoglycosides, to fluoroquinolones, nitrofurantoin, chloramphenicol and trimethoprim–sulphamethoxazole. The MICs of tigecycline and colistin of isolate A measured by E-test were 0.25 and 0.094 mg/L, respectively, whereas those of isolate B were 0.25 and 4 mg/L, respectively.

EŞ

J Antimicrob Chemother 2011; 66: 657–663
doi:10.1093/jac/dkq494 Advance Access publication 29 December 2010

Journal of Antimicrobial Chemotherapy

Bacteraemia due to multidrug-resistant Gram-negative bacilli in cancer patients: risk factors, antibiotic therapy and outcomes

C. Gudiol[1,2*], F. Tubau[3,4], L. Calatayud[3,4], C. Garcia-Vidal[1,2], M. Cisnal[3], I. Sánchez-Ortega[5], R. Duarte[5], M. Calvo[6] and J. Carratalà[1,2]

- **4 yıl, prospektif, 747 bakteremi**
- **%49.9 GNB, %13.7 MDR**
- ***E.coli* - ESBL(+); %45, Amp-C aşırı yapımı; %24**
- **Yetersiz tedavi olasılığı %69 ve %9**
- **Mortalite %41 ve %21**

KARBAPENEM DİRENÇLİ GNB – ERKEN KARBAPENEM?

- ***A.baumanii*** **ve MDR -** ***P.aeruginosa***
- ***S.maltophilia***
- **KARBAPENAMAZ -** ***Enterobactericeae***

  Metallo-β-laktamaz (VIM, IMP)

  Oxa-β-laktamaz (OXA-48)

  Class A KPC

KARBAPENEM DİRENÇLİ GNB

Hematolojik malignitelerden izole edilen

***P.aeruginosa* - %30-70'i MDR, %25-60'ı**

Karba-R

- *Caselli, et al. Hamatologica 2010*
- *Trecarichi EM, et al. Hematologica 2011*

Available online at www.sciencedirect.com
ScienceDirect
Diagnostic Microbiology and Infectious Disease 70 (2011) 367–372
DIAGNOSTIC MICROBIOLOGY AND INFECTIOUS DISEASE
www.elsevier.com/locate/diagmicrobio

Antimicrobial Susceptibility Studies

The effects of group 1 versus group 2 carbapenems on imipenem-resistant *Pseudomonas aeruginosa*: an ecological study☆

Yehuda Carmeli*, Shiri Klarfeld Lidji, Esther Shabtai, Shiri Navon-Venezia, Mitchell J. Schwaber

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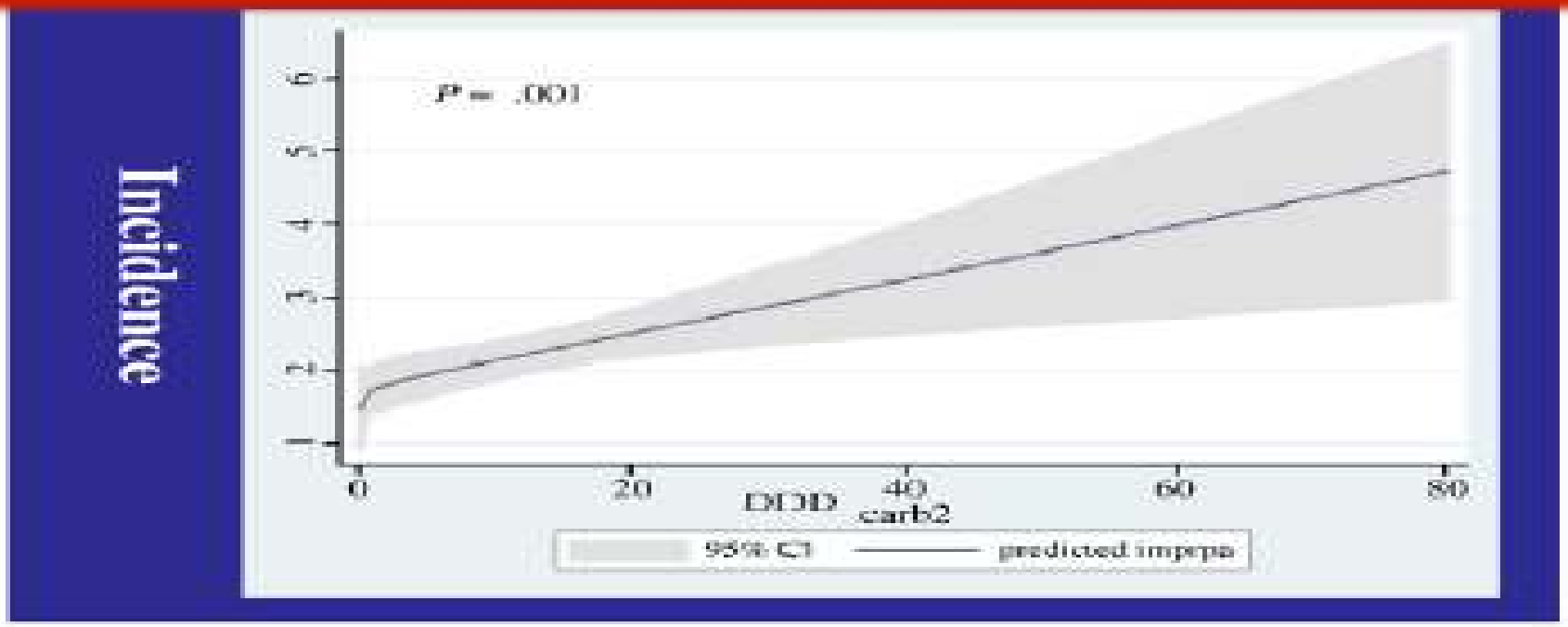
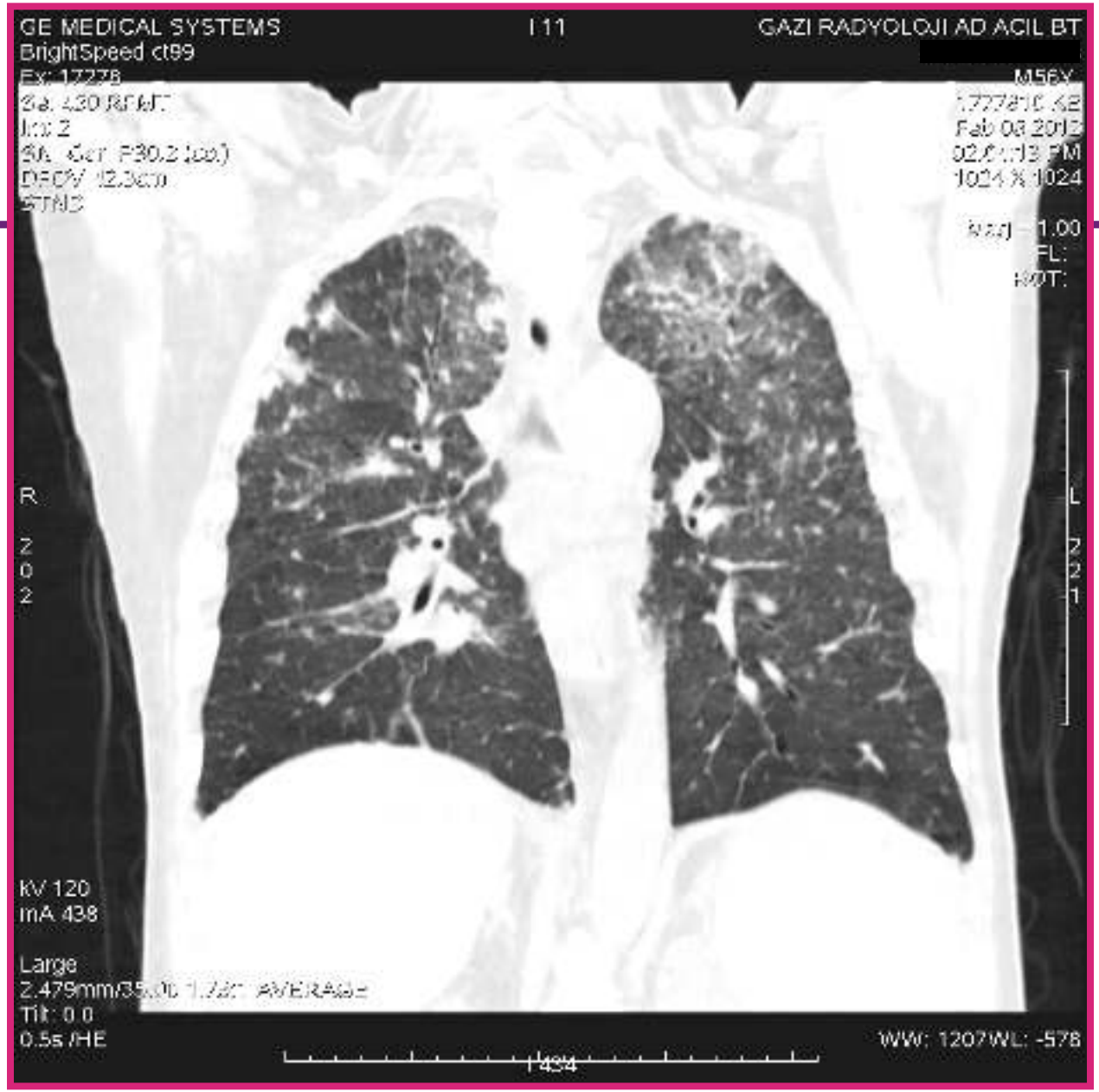
Received 16 December 2010; accepted 13 March 2011

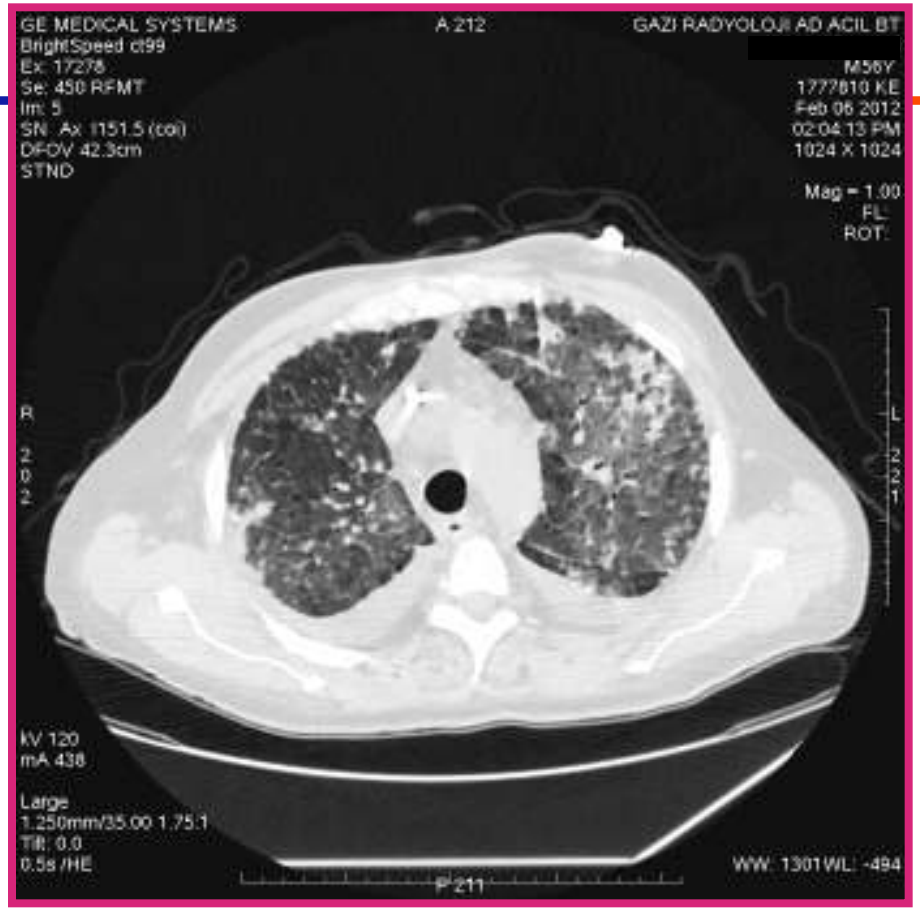
Abstract

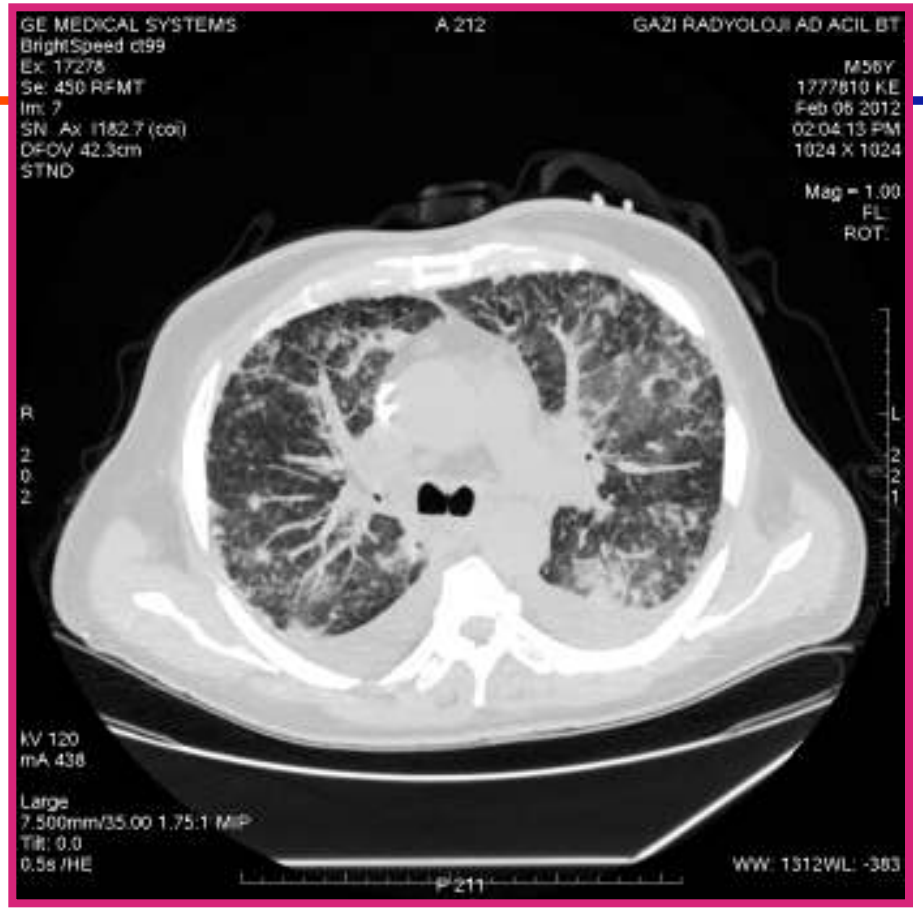
Use of the group 2 carbapenems, imipenem and meropenem, may lead to emergence of *Pseudomonas aeruginosa* resistance. The group 1 carbapenem ertapenem has limited activity against *P. aeruginosa* and is not associated with imipenem-resistant *P. aeruginosa* (IMP-R PA) in vitro. This retrospective, group-level, longitudinal study collected patient, antibiotic use, and resistance data from 2001 to 2005 using a hospital database containing information on 9 medical wards. A longitudinal data time series analysis was done to evaluate the association between carbapenem use (defined daily doses, or DDDs) and IMP-R PA. A total of 139 185 patient admissions were included, with 541 150 antibiotics DDDs prescribed: 4637 DDDs of group 2 carbapenems and 2130 DDDs of ertapenem. A total of 779 IMP-R PA were isolated (5.6 cases/1000 admissions). Univariate analysis found a higher incidence of IMP-R PA with group 2 carbapenems ($P < 0.001$), aminoglycosides ($P = 0.034$), and penicillins ($P = 0.05$), but not with ertapenem. Multivariate analysis showed a yearly increase in incidence of IMP-R-PA (3.8%, $P < 0.001$). Group 2 carbapenem use was highly associated with IMP-R PA, with a 20% increase in incidence ($P = 0.0014$) for each 100 DDDs. Group 2 carbapenem use tended to be associated with an increased proportion of IMP-R PA ($P = 0.0625$) in multivariate analysis. Ertapenem was not associated with IMP-R PA. These data would support preferentially prescribing ertapenem rather than group 2 carbapenems where clinically appropriate.





Noduler infiltratların eşlik ettiği buzlu cam infiltrasyonu





Her iki üst lob superior segmentlerde yamasal buzlu cam alanları, eşlik eden buzlu cam ve interloküler septal kalınlaşmalar

OLGU

- **Persistan NÖTROPENİK ATEŞ-AML :İmipenem + Teikoplanin**
- **Hipotansiyon, hipotermi ve karın distansiyonu**
- **HRCT'de yaygın buzlu cam alanları**
- **YBÜ**
- **Hastanın kateter ucu kültüründe: *K. pneumoniae* üremesi oluyor.**
- **Antibiyotik duyarlılığı: sadece Amikasin, Tigesiklin ,Doripenem E test saptanıyor**

Multidrug-Resistant Bacterial Organisms Causing Major Clinical Problems.*

Organism and Antibiotic Resistance	Common Mechanism of Resistance	Recent, Resurrected, and Future Antimicrobial Agents with Potential Clinical Use
Hospital-associated MRSA†		
Vancomycin (both VISA and VRSA)	Thickening of cell wall (not fully elucidated); change in the last amino acid of peptidoglycan precursors	Linezolid, quinupristin–dalfopristin, daptomycin, tigecycline, ceftobiprole, ceftaroline, dalbavancin, telavancin, oritavancin, iclaprim
Daptomycin	Associated with changes in cell wall and cell membrane (not fully elucidated)	Linezolid, quinupristin–dalfopristin, tigecycline, ceftobiprole, ceftaroline, dalbavancin, telavancin, oritavancin, iclaprim
Linezolid	Mutations in the 23S ribosomal RNA genes; rarely, acquisition of a methyltransferase gene (*cfr*)	Daptomycin, quinupristin–dalfopristin, tigecycline, ceftobiprole, ceftaroline, dalbavancin, telavancin, oritavancin, iclaprim
Vancomycin-resistant *Enterococcus faecium*†		
Ampicillin (common)	Mutation and overexpression of *pbp5*	Linezolid, quinupristin–dalfopristin, daptomycin, tigecycline
High-level resistance to aminoglycosides	Acquisition of aminoglycoside-modifying enzymes; ribosomal mutations (streptomycin)	No alternative for a reliable bactericidal effect alone or in combination
Linezolid	Mutations in the 23S ribosomal RNA genes	Quinupristin–dalfopristin, daptomycin, tigecycline
Daptomycin	Unknown	Linezolid, quinupristin–dalfopristin, tigecycline
	Enzymes that inactivate quinupristin–dalfopristin, target modification	Daptomycin, linezolid, tigecycline
Escherichia coli, klebsiella species, and enterobacter species§		
Oxyimino-cephalosporins (ceftriaxone, cefotaxime, ceftazidime, and cefepime)	Extended-spectrum β-lactamases (includes hyperproduction of the AmpC enzymes by Enterobacteriaceae family)	Carbapenems, tigecycline
Carbapenems	Production of carbapenemases, decreased	Polymyxins, tigecycline
Acinetobacter species¶		
Carbapenems	Decreased permeability, increased efflux, and production of carbapenemases	Polymyxins
Pseudomonas aeruginosa¶		
Carbapenems	Decreased permeability, increased efflux, and production of carbapenemases	Polymyxins

KOLİSTİN-SORUNLAR?

- **Parenteral polymyxin B: %14 renal yetmezlik (bazal serum kreatinin düzeyleri normal) %57 mortalite**

Quaderkirk JP. Antimicrob Agents Chemother 2003

- **Nefrotoksisite: %27-58**
- **Pnömonide kolistin; %75 başarısızlık**

Levin AS. Clin Infect Dis 1999

- **PK/PD ?, konsantrasyon-bağımlı, standart dozlar ile R gelişimi, 4 gün sonra, yüksek doz gereksinimi ?**

Tam VH. Antimicrob Agents Chemother 2003

- ***Duyarlılığı azalmış P. aeruginosa***
- ***Acinetobacter*; heterorezistans - kolistin**

Landman D. J Antimicrob Agents Chemother 2005

EŞ

Li J.Antimicrob Agents Chemother 2006

Mediterranean Journal of Hematology and Infectious Diseases

Review Article

New Insight on Epidemiology and Management of Bacterial Bloodstream Infection in Patients with Hematological Malignancies

Sara Lo Menzo*, Giulia la Martire*, Giancarlo Ceccarelli and Mario Venditti.

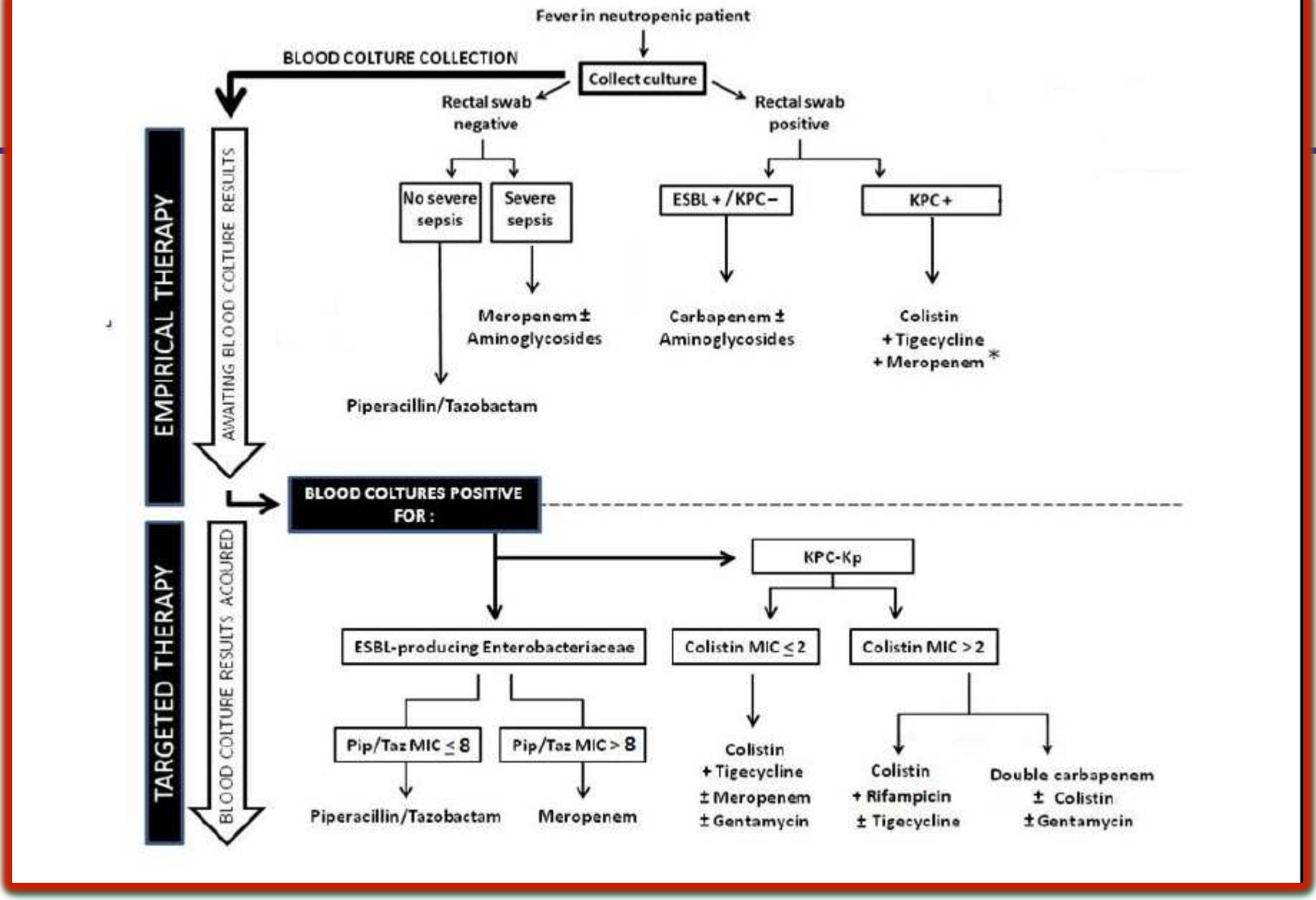
Department of Public Health and Infectious Diseases. University of Rome "Sapienza", Rome (Italy)
* These authors contributed equally to this paper

Abstract. Bloodstream infections (BSI) are a significant cause of morbidity and mortality in onco-hematologic patients. The Gram-negative bacteria were the main responsible for the febrile neutropenia in the sixties; their impact declined due to the use of fluoroquinolone prophylaxis. This situation was followed by the gradual emergence of Gram-positive bacteria also following the increased use of intravascular devices and the introduction of new chemotherapeutic strategies. In the last decade, the Gram-negative etiology is raising again because of the emergence of resistant strains that make questionable the usefulness of current strategies for prophylaxis and empirical treatment. Gram-negative BSI attributable mortality is relevant, and the appropriate empirical treatment significantly improves the prognosis; on the other hand the adequate delayed treatment of Gram-positive BSI does not seem to have a high impact on survival. The clinician has to be aware of the epidemiology of his institution and colonizations of his patients to choose the most appropriate empiric therapy. In a setting of high endemicity of multidrug-resistant infections also the choice of targeted therapy can be a challenge, often requiring strategies based on off-label prescriptions and low grade evidence.

In this review, we summarize the current evidence for the best targeted therapies for difficult to treat bacteria BSIs and future perspectives in this topic. We also provide a flow chart for a rational approach to the empirical treatment of febrile neutropenia in a multidrug resistant, high prevalence setting.

Citation: Lo Menzo S., la Martire G., Ceccarelli G., Venditti M. New insight on epidemiology and management of bacterial bloodstream infection in patients with hematological malignancies. Mediterr J Hematol Infect Dis 2015, 7(1): e2015044, DOI: http://dx.doi.org/10.4084/MJHID.2015.044

Published: July 01, 2015, **Received: April 28, 2015,** **Accepted: June 08, 2015**


Fever in neutropenic patient
BLOOD COLTURE COLLECTION
Collect culture
Rectal swab negative
Rectal swab positive
No severe sepsis
Severe sepsis
ESBL + / KPC –
KPC +
Meropenem ± Aminoglycosides
Carbapenem ± Aminoglycosides
Colistin + Tigecycline + Meropenem *
Piperacillin/Tazobactam
EMPIRICAL THERAPY
AWAITING BLOOD COLTURE RESULTS
BLOOD COLTURES POSITIVE FOR :
TARGETED THERAPY
BLOOD COLTURE RESULTS ACQUIRED
KPC-Kp
ESBL-producing Enterobacteriaceae
Colistin MIC ≤ 2
Colistin MIC > 2
Pip/Taz MIC ≤ 8
Pip/Taz MIC > 8
Colistin + Tigecycline ± Meropenem ± Gentamycin
Colistin + Rifampicin ± Tigecycline
Double carbapenem ± Colistin ± Gentamycin
Piperacillin/Tazobactam
Meropenem

O ZAMAN ÇÖZÜM BEKLEYEN ?

- Başlangıç tedavinin yetersiz kalabileceği hasta grupları tanımı
- Monoterapi?
- Kinolon profilaksisi?
- Dirençli gram pozitifler için başlangıç tedavi

ÇÖZÜM BEKLEYEN ?

- Artan direnç eşliğinde empirik tedavi
- Karbapenemlerin kısıtlı kullanım önerileri eşliğinde eskalasyon ve de-eskalasyon
- MDR riski olan alt grupların tanımlanması
- Takım çalışması
- MDR - tedavi seçenekleri ile ilişkili klinik veri

J Antimicrob Chemother 2011; **66** Suppl 1: i55–58
doi:10.1093/jac/dkq442

Journal of Antimicrobial Chemotherapy

Managing invasive fungal infections: relying on clinical instincts or on a rational navigation system?

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The management of invasive fungal disease in the immunocompromised host is complex and requires the specialized knowledge of physicians whose primary interest is actually the underlying disease rather than infectious complications. This Supplement aims to provide these physicians with some tools that may help to guide them through the maze of suspicion that an invasive fungal disease is present by offering an integrated care pathway of rational patient management. Such pathways will inevitably vary in detail in different centres and depend for their success on the presence of multidisciplinary teams and an explicit agreement on at least the minimum requirements for effective management. The integrated care pathways presented constitute an objective instrument to allow regular audits for recognizing opportunities to change practice if and when weaknesses are identified.

Keywords: invasive fungus, guidelines, antifungal therapy, immunodeficiency

BİZİM TAKIM

Pulmonolog

Antifungal Seçimini Etkileyen Faktörler

- Risk of nephrotoxicity (eg, higher patient age, concomitant nephrotoxic drugs, or renal impairment)
- Liver dysfunction
- Ability for oral medication—gastrointestinal function (mucositis, nausea, and vomiting)
- Active leukemia and plans for hemopoietic transplant
- Type of chemotherapy (remission induction vs consolidation vs palliation)
- Type of fungus
- Site of infection (eg, central nervous system disease)
- Certainty of diagnosis
- Interactions of concomitant drugs with antifungals
- Infected hardware or catheters
- Prior antifungal exposure (risk of cross-resistance or tolerance with azoles)
- Refractory IFI and number of previously failed regimens
- Patient's preference and ability to pay for oral antifungals
- Immunosuppression and reconstitution (timing and intensity of immunosuppression)
- Concomitant infections (cytomegalovirus or bacteria) and their treatment
- Patient's compliance
- Outpatient vs inpatient treatment

CID 2010;50:405-415

ANTİFUNGAL SEÇİMİNİ ETKİLEYEN FAKTÖRLER !!!

GK SUT EK-4/G Parenteral formları; sadece yatan hastalarda kullanılması halinde bedelleri ödenir.

4.2.23 - Amfoterisin-B, kaspofungin, anidilofungin, vorikonazol, posakonazol, ıtrakonazol (infüzyon ve solüsyon) kullanım ilkeleri

(1) Hastanın böbrek ve karaciğer fonksiyonları normal ise ilk tercih klasik amfoterisin-B veya flukonazoldür.

(2) Klasik amfoterisin-B'ye alerjik reaksiyon gösterdiğinin uzman hekim raporu ile belgelenmesi ya da hastanın karaciğer veya böbrek fonksiyon testlerinin laboratuvar verileri ile bozuk olduğunun belgelenmesi halinde lipozomal veya lipid kompleks veya kolloidal dispersiyon amfoterisin-B veya kaspofungin veya anidilofungin veya posakonazol veya vorikanazol veya ıtrakonazol (infüzyon) kullanılabilir.

(3) Itrakonazol solüsyon;
a) HIV pozitif veya bağışıklığı bozulan hastalardaki flukonazole dirençli özofajiyal kandidozun tedavisinde kullanılır.
b) Hematolojik malignitesi olan veya kemik iliği transplantasyonu yapılan ve nötropeni geliştirmesi beklenen (<500 hücre/ml) hastalardaki derin fungal (mantar) enfeksiyonlarının profilaksisinde kullanılır.
c) Itrakonazol'un oral formları (Solüsyon formları hariç), SUT eki "Sistemik Antimikrobik ve Diğer İlaçların Reçeteleme Kuralları Listesi" nin (EK-4/E) 10.5 maddesinde belirtildiği şekilde reçetelenebilecektir.

(4) Posakonazol;
a) Aşağıda tanımlanan hastalardaki invazif mantar enfeksiyonlarının profilaksisinde kullanılır. (Yukarıda yer alan birinci ve ikinci fıkra hükümleri aranmaz.)
1) İnvazif mantar enfeksiyonu gelişme riski yüksek olan ve uzun süreli nötropeni oluşabileceği düşünülen akut miyeloid lösemi (AML) veya miyelodisplastik sendrom (MDS) nedeniyle remisyon-indüksiyon kemoterapisi alan hastalarda.
2) İnvazif mantar enfeksiyonu gelişme riski yüksek olan ve Graft versus host hastalığına yönelik olarak yüksek doz immünsupresif tedavi alan allojenik hematopoetik kök hücre transplantı (HSCT) alıcısı olan hastalarda.
b) Tedavi amaçlı olarak aşağıda tanımlanan durumlarda kullanılır.
1) İmmun yetmezliği olan flukonazole dirençli orofarengeal kandiyazis tedavisinde.
2) Amfoterisin B, lipozomal amfoterisin B veya vorikonazol tedavilerine refrakter invazif aspergilozis tedavisinde.
3) Amfoterisin B ile tedaviye refrakter ya da amfoterisin B'yi tolere edemeyen fusariozis hastalığı olan hastalarda.
4) Itrakonazol ile tedaviye refrakter ya da itrakonazol'u tolere edemeyen kromoblastomikoz ve micetoma hastalığı olan hastalarda.
5) Amfoterisin B ya da ıtrakonazol veya flukonazol ile tedaviye refrakter ya da bu tıbbi ürünleri tolere edemeyen koksidiodomikoz hastalığı olan hastalarda.

(5) Anidulofungin, nötropenik olmayan (Mutlak nötrofil sayısı ≥ 500/mm3 olacak ve laboratuvar sonucu aranacaktır.) erişkin hastalarda, invazif kandidiyazis vakalarında reçetelendirilebilir.

(6) Lipozomal amfoterisin-B, lipid kompleks veya kolloidal dispersiyon amfoterisin-B'nin parenteral formları, kaspofungin, anidilofungin, vorikanazol, posakonazol veya ıtrakonazol (infüzyon) yukarıdaki şartları sağlayan uzman hekim raporu ve enfeksiyon hastalıkları uzmanı onayı ile yatarak tedavide kullanılır. Bu ilaçların oral formları ise enfeksiyon hastalıkları uzmanınca düzenlenecek uzman hekim raporuna dayanılarak tüm uzman hekimlerce reçetelenmesi halinde ayakta tedavide de kullanılabilecektir.

SGK SUT EK-4/G Sadece yatan hastalarda kullanılması halinde bedelleri ödenir.

Aradığınız bilgiye ulaşamadıysanız, etkin maddesi aynı olan aşağıdaki ilaçların prospektüs, kullanım talimatı ve kısa ürün bilgilerinden faydalanabilirsiniz.

AMPHO B EFFECT

If this is the cure, I'll go for the disease…..

ANTİFUNGALLERİN SIK KARŞILAŞILAN TOKSİSİTELERİ

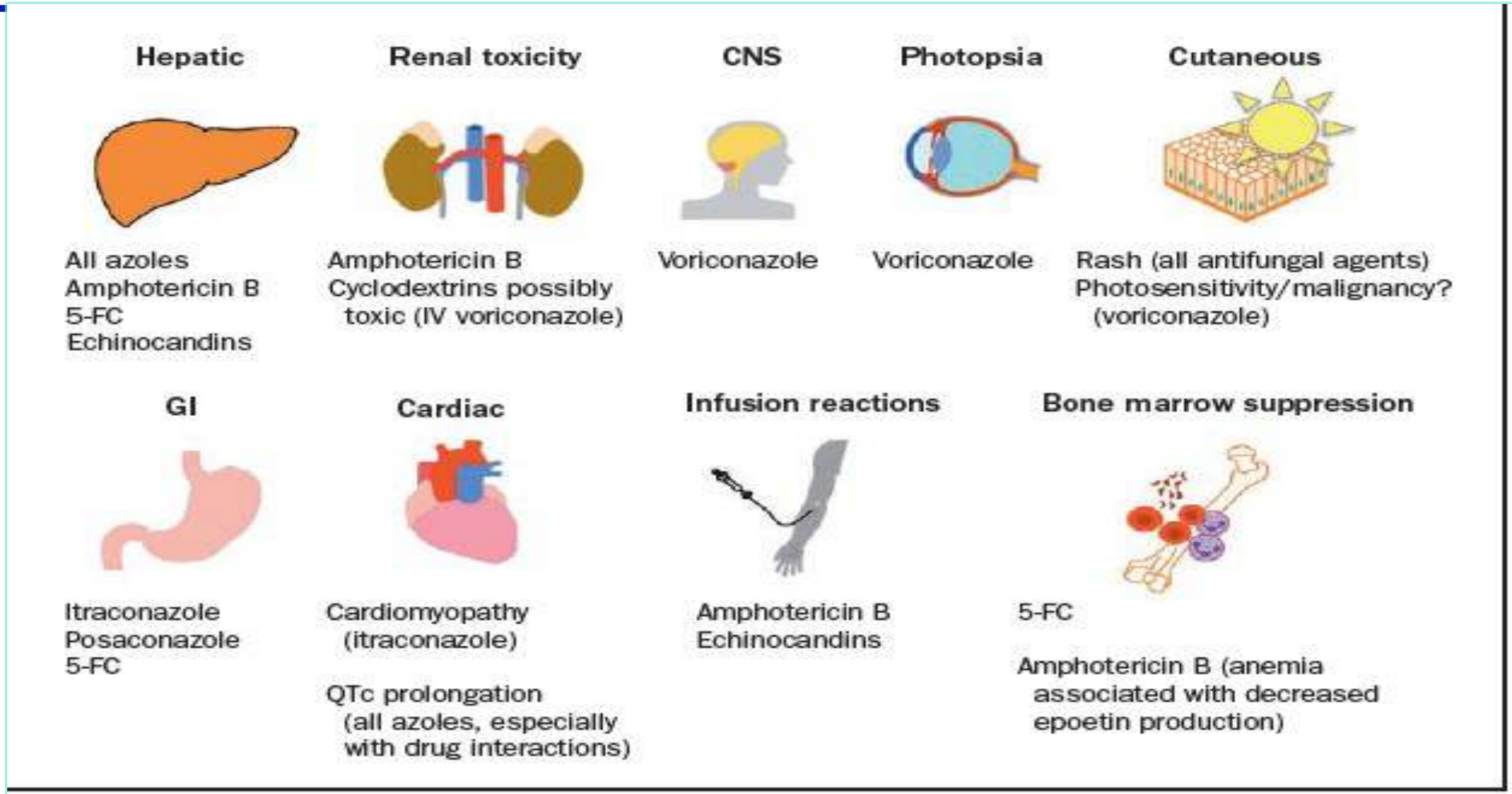

FIGURE 4. Common toxicities of antifungal agents. CNS = central nervous system; 5-FC = flucytosine; GI = gastrointestinal; IV = intravenous; QTc = corrected QT interval.

Evaluation of the Practice of Antifungal Prophylaxis Use in Patients With Newly Diagnosed Acute Myeloid Leukemia: Results From the SEIFEM 2010-B Registry

Livio Pagano,[1] Morena Caira,[1] Anna Candoni,[2] Franco Aversa,[3] Carlo Castagnola,[4] Ce
Mario Delia,[7] Maria Rosaria De Paolis,[8] Roberta Di Blasi,[1] Luigi Di Caprio,[9] Rosa Fa
Bruno Martino,[12] Lorella Melillo,[13] Maria Enza Mitra,[14] Gianpaolo Nadali,[15] Annamar
Leonardo Potenza,[18] Prassede Salutari,[19] Enrico Maria Trecarichi,[20] Mario Tumbarel
Nicola Vianelli,[22] and Alessandro Busca;[23] for the SEIFEM Group*

Clin Infect Dis

Background. To analyze the efficacy of antifungal prophylaxis (AFP) with posaconazole and itraconazole in a real-life setting of patients with acute myeloid leukemia (AML) during the first induction of remission.

Methods. From January 2010 to June 2011, all patients with newly diagnosed AML were consecutively registered and prospectively monitored at 30 Italian hematological centers. Our analysis focused on adult patients who received intensive chemotherapy and a mold-active AFP for at least 5 days. To determine the efficacy of prophylaxis, invasive fungal disease (IFD) incidence, IFD-attributable mortality, and overall survival were evaluated.

Results. In total, 515 patients were included in the present analysis. Posaconazole was the most frequently prescribed drug (260 patients [50%]) followed by fluconazole (148 [29%]) and itraconazole (93 [18%]). When comparing the groups taking posaconazole and itraconazole, there were no significant differences in the baseline clinical characteristics, whereas there were significant differences in the percentage of breakthrough IFDs (18.9% with posaconazole and 38.7% with itraconazole, $P < .001$). The same trend was observed when only proven/probable mold infections were considered (posaconazole, 2.7% vs itraconazole, 10.7%, $P = .02$). There were no significant differences in the IFD-associated mortality rate, while posaconazole prophylaxis had a significant impact on overall survival at day 90 ($P = .002$).

Conclusions. During the last years, the use of posaconazole prophylaxis in high-risk patients has significantly increased. Although our study was not randomized, it demonstrates in a real-life setting that posaconazole prophylaxis confers an advantage in terms of both breakthrough IFDs and overall survival compared to itraconazole prophylaxis.

Posakonazol- AML

	Years	Type	N° pts	IFDs	incidence%
RCT					
Cornelly et al, NEJM 2007	2002-05	RCT	304	7	2%
"Real life" series					
Michallet et al, Med Mycol 2011	2007-08	Pros	55	2	3.6%
Candoni et al, EHA 2011	2009-10	Retro	55	2	4%
Lerolle et al, ICAAC 2011	2007-10	Retro	209	8	3.8%
Hahn et al, Mycoses 2011	2007-08	Retro	21	1	5%
Egerer et al, Mycoses 2011	2007-09	Retro	76	1	1.3%
Vehreschild et al, JAC 2010	2006-08	Retro	77	3	3.9%
Busca et al, 5th TIMM 2011	2009-10	Retro	61	0	0
Ananda-Rajah, Haematol 2012	2006-10	Retro	68	0	0
Peterson et al, Mycoses 2013	2006-10	Retro	100	4	4%
ALL STUDIES			**722**	**21**	**2.9%**

Pagano et al. Haematologica 2012

PROFİLAKSİ - İZLEM

- IFI insidansı-epidemiyolojisi
- Empirik Antifungal Tedavi gereksinimi
- Toksisite
- Serum düzeyleri

THE EPIDEMIOLOGY OF INVASIVE FUNGAL INFECTIONS IN CANCER PATIENTS: A NATIONWIDE TURKISH FUNGAL REGISTRY STUDY

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Keywords: Epidemiology, Fungal infection, Cancer patients

Objectives: The evidence regarding the epidemiology of invasive fungal infections (IFIs) is limited in Turkey where major risk factors such as cancer, organ transplant and HSCT have considerably increased in the last decade. We aimed to assess the epidemiological characteristics and outcome of invasive fungal infections in cancer patients with specific regard to fungal etiology in Turkey.

Methods: The study was a prospective, observational, multicenter study. Patients admitted to hematology and oncology clinics of ten participating centers receiving treatment for cancer and/or stem cell transplantation (SCT) with a diagnosis of probable/proven IFI based on the revised definitions of EORTC/MSG were enrolled to the study for the duration of two years from July 2013 to July 2015. Demographic and relevant medical data was collected by a web-based electronic data capture system by the investigator of each center. All fungal episodes were analyzed according to the primary endpoint defined as the distribution of main fungal pathogens and species. Patients underwent an optional six-week follow-up period. At the 6th week visit, outcome defined as the treatment response and mortality with specific regard to fungal species were analysed.

Results: A total of 112 patients with mean age of 46.2±1.5 years were enrolled to the study and 86 of them completed the 6th week follow-up and outcome analysis. Most of the patients (90%) had an underlying hematological malignancy and 78.6.% had neutropenia. The diagnosis of IFI was proven in 47.3% and probable in 52.7% of the patients. Predominant pathogens for culture-positive cases were *Candida spp* (27/53, 50.9%) and *Aspergillus spp* (15/53, 28%) with mortality rates of 37% (10/27) and 26.7% (4/15) respectively. Crude mortality rate at 6th week for all IFIs was 20.5% (23/112) with mortality rates for proven and probable cases of 32.1% (17/53) and 10.2% (6/59) respectively. The most common site of involvement was defined to be the lungs (43.4%) and bloodstream (28.3%) for proven cases and lung (94.9%) for probable cases. 55/112 patients were recieving antifungal prophylaxis before IFIs defined with 56% of the prophylaxis was with antimold agents. Although the distribution of fungal species were not found to be influenced with the previous antimold prophylaxis, proven IFIs were more prominent among the patients recieving fluconazole patients.(70.8% vs 35.5% p:0.014). Voriconazole (50.9%), liposomal amphotericin B (34.8%) and caspofungin (28.6%) were the most frequently administered antifungals. Treatment responses were defined as complete, partial or stable in 68.8% of cases where in 8% of patients treatment failure leading to need in change of antifungal therapy was reported.

Conclusions: This was the first nationwide IFI epidemiology study in Turkey revealing important data regarding the epidemiology of strictly defined IFIs in a cohort of high-risk hematological malignancies.Despite all the efforts and good clinical practice still 1 out of 5 high-risk patients are died due to IFIs.

Pathogen	n(%)
Aspergillus	15(28,3)
Aspergillus Niger	2(13,3)
Aspergillus fumigatus	7(46,6)
Aspergillus Flavus	4(26,6)
Asperrgillus spp	2(13,3)

Candidas	n(%)
Candida	27 (50,9)
Candida Non-Albicans	17 (32,0)
Candida Parapsilosis	2(3,7)
Candida Cruise	4(7,5)
Candida Glabrata	6(11,3)
Candida Kefyr	4(7,5)
Candida Spp	1(1,9)
Candida Albicans	10 (18,9)

NAC : 17/27: %63

Other	n(%)
Mukormukozis	2(3,8)
Pesilomices	1(1,9)
Trichosporon	2(3,8)
Fusarium	2 (3,8)
Rhizopus	1 (1,9)
Derin Mantar Enfeksiyonu	1 (1,9)
Küf	2 (3,8)

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Original article

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Epidemiology of candidaemia in a tertiary care university hospital: 10-year experience with 381 candidaemia episodes between 2001 and 2010

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Summary

Defining the epidemiology of and risk factors for candidaemia is necessary to guide empirical treatment. The objectives of this study were to determine the ranking of *Candida* among positive blood cultures, to define the epidemiology of candidaemia and to investigate patient characteristics and their relationship with *C. albicans* vs. non-*albicans Candida* (NAC) candidaemia. Candidaemia episodes between January 2001 and December 2010 were evaluated retrospectively. Patient characteristics were compared across *Candida* species. *Candida* ranked as the fifth most frequently isolated pathogen. Among 381 candidaemia episodes, 58.3% were due to *C. albicans*, followed by *C. parapsilosis* (15.2%), *C. tropicalis* (13.4%) and *C. glabrata* (6.8%). No statistically significant difference was observed in the distribution of *C. albicans* vs. NAC ($P = 0.432$). Patients with NAC had significantly higher rates of haematological disorders ($P < 0.001$) and neutropenia ($P = 0.003$), and were older ($P = 0.024$) than patients with *C. albicans*, whereas patients with urinary catheters had higher rates of *C. albicans* ($P = 0.007$). On species basis, *C. tropicalis* was more frequently isolated from patients with haematological disorders ($P < 0.001$) and neutropenia ($P = 0.008$). Patients with urinary catheters were less likely to have *C. parapsilosis* ($P = 0.043$). *C. glabrata* was most prevalent among patients with solid organ tumours ($P = 0.038$), but not evident in patients with haematological disorders. Local epidemiological features and risk factors may have important implications for the management of candidaemia.

ÖZETLE

- UZLAŞI RAPORLARI
- EPİDEMİYOLOJİK VERİ-ÇOK MERKEZLİ ÇALIŞMA
- ANTİBİYOTİK SEÇENEKLERİ-TOKSİSİTE ? ETKİNLİK
- PK/PD PARAMETRELERİN KULLANILMASI

BAŞLA

YENİDEN BAŞLA

Gerçek Hikaye

Gerçek yaşam

Randomize Klinik Çalışmalar

Rehberler

IDSA GUIDELINES

Clinical Infectious Diseases 2014;58(3):e44–100

2013 IDSA Clinical Practice Guideline for Vaccination of the Immunocompromised Host

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- **KİM SORUMLU?**
- **NE ZAMAN?**
  - **İMMUNSUPRESYONDAN ÖNCE**
  - **İNAKTİF AŞILAR ≥2, CANLI AŞILAR≥4 HAFTA**
- **AİLE/YAKINLARININ AŞILANMASI**
- **SEYAHAT**

DİNLEDİĞİNİZ İÇİN TEŞEKKÜRLER…

SORULARINIZ?

Prof. Dr. Esin Şenol