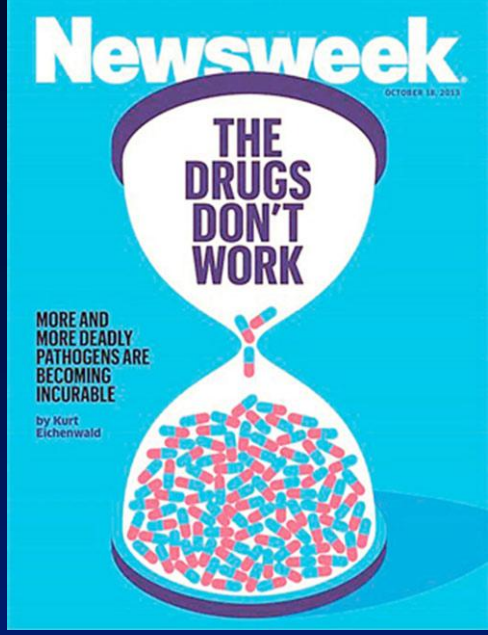


Global KRİZ (Dirençli Gram Negatifler) Elimizde ne kaldı?

Dr Gökhan AYGÜN
İÜ CTF Tıbbi Mikrobiyoloji AD

Sunum

- Sorun?
- Sorun mikroorganizmalar
- Kısıtlı seçenekler ? (kolistin, tigesiklin,…)
- Akılcı tedavi ?
- ESBL : sorunun başlangıcı !!!
- Gelecek !!!
- Sonuç

Çoklu Dirençli GNÇ İnfeksiyonlarının Akılcı Tedavisi SORUN?

TIME
IN PARTNERSHIP WITH CNN

Thursday, Oct. 01, 2009

The Desperate Need for Antibiotics

By Eben Harrell / London

In recent years, efforts... hospital-acquired infe... antibiotics available to... have neglected to inve...

Bacterial and parasitic... antibiotic research rel... deaths attributed to h... drug-resistant "superb...

THE NEW YORKER

MEDICAL DISPATCH

SUPERBUGS

...impossible to treat.

Drug-resistant bacteria kills thousands in U.S.

Study finds 85 percent of invasive infections linked to health-care centers

By Kevin Sack
New York Times

ATLANTA: Nearly 19,000 people died in the United States in 2005 after being infected with virulent drug-resistant bacteria that have spread rampantly through hospitals and nursing homes, according to the most thorough study of the disease's prevalence ever conducted.

The government study, which appears today in the Journal of the American Medical Association, suggests such common as previously thought, according to its lead author, Dr. R. Monina Klevens.

If the mortality estimates are correct, the number of deaths associated with the germ, methicillin-resistant Staphylococcus aureus, or MRSA, would exceed those attributed to HIV-AIDS, Parkinson's disease, emphysema or homicide each year.

By extrapolating data collected in nine locations, the researchers estimated that 94,360 patients developed an invasive infection from the pathogen in 2005 and that nearly one of every five, or 18,650 of them, died. The study points out that it is not always possible to determine whether a death is caused by MRSA or merely accelerated by it.

The authors, who work for the U.S. Centers for Disease Control and Prevention, cautioned that their methodology differed significantly from pre-

Doctors fear that dangerous bacteria may become

BBC NEWS

Home UK Africa Asia

16 November 2012 Last up...

Antibiotic resistance 'big threat to health'

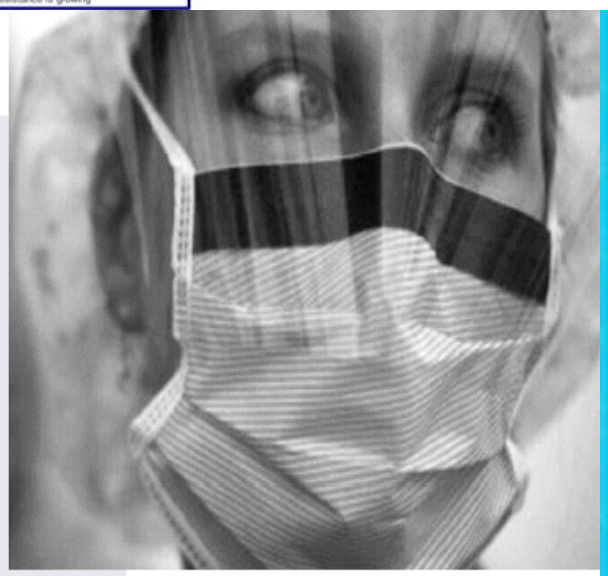
COMMENTS (444)

Resistance to antibiotics is one of the greatest threats to modern health, experts say.

The warning from England's chief medical officer and the Health Protection Agency comes amid reports of growing problems with resistant strains of bugs such as E. coli and gonorrhoea.

They said many antibiotics were being used unnecessarily for mild infections, helping to...

Antibiotic resistance is growing



"Infectious diseases physicians are alarmed by the prospect that effective antibiotics may not be available to treat seriously ill patients in the near future. There simply aren't enough new drugs in the pharmaceutical pipeline to keep pace with drug-resistant bacterial infections, so-called 'superbugs.'"

Joseph R. Dalovisio, MD
IDSA President

Newsweek

OCTOBER 18, 2013

THE DRUGS DON'T WORK

...RE AND MORE DEADLY PATHOGENS ARE BECOMING INCURABLE

by Kurt Eichenwald

Sorun (MDR) Bakteriler

- *ESBL/GSBL E.coli, Klebsiella*
- *KARBAPENEMAZ (CRE)*
- *P. aeruginosa*
  - İmipenem ve seftazidime ve amikasin ve siprofloksasin
- *Acinetobacter spp. (PANR)*
  - İmipenem

TÜRKİYE'DE DİRENÇ SORUNU BÜYÜYOR

KAN KÜLTÜRLERİ (n=594), 16 Merkez	Karbapenem Direnci (%)
Acinetobacter sp.	94
Pseudomonas sp.	47
Klebsiella sp.	38
E.coli	9
Enterobacter sp.	8

!!!

Ulusal Sağlık Bakımı İnfeksiyonları Simpozyumu, USBİS 2014,İstanbul

Karbapenemaz !

- Metallo beta laktamazlar (VIM, IPM, NDM-1,…)
- KPC enzimleri

  (K.pneumoniae …ABD)
- TEM, SHV ya da ampC enzimler +

  OMP defektleri
- OXA + OMP defektleri
- ???

Country	Types of detected carbapenemase			
Author/year	OXA	VIM	KPC	NDM-1
Lebanon				
Matar et al./2008	48			
Matar et al./2010	48			
El-Herte et al./2012	48			+
Turkey				
Poirel et al./2004	+1,47,48			
Gaçar et al./2005		5		
Aktaş et al./2008	48			
Gülmez et al./2008	48			
Carrer et al./2008	48			
Carrer et al./2010	48			
Egypt				
Cuzon et al./2009	48			
Kuwait				
Jamal et al./2011				+
Oman				
Poirel et al./2010				+
Saudi Arabia				
Guerin et al./2005	48			
Israel				
Navon-Venezia et al./2006			2	
Leavitt et al./2007			3	
Lopez et al./2010			3	
Greece				
Giakkoupi et al./2003		1		
Loli et al./2006		1		
Ikonomidis et al./2007		4		
Ikonomidis et al./2007		+1/+2		
		12		
Psichogiou et al./2008		1		
Tsakris et al./2008			2	
Tokatlidou et al./2008		12		
Giakkoupi et al./2009		1	2	
Giakkoupi et al./209			2	
Pournaras et al./2009			2	
Hawser et al./2009			KPC not subtyped	
Pournaras et al./2010		19	2	
Kontopoulou et al./2010			2	
Zioga et al./2010		1	2	

Antibiyotik direncinin bedeli

- Maliyet artışı
- Hastanede daha uzun süre kalış
- Artmış mortalite

Clinical Infectious Diseases 2006; 42:S82–9

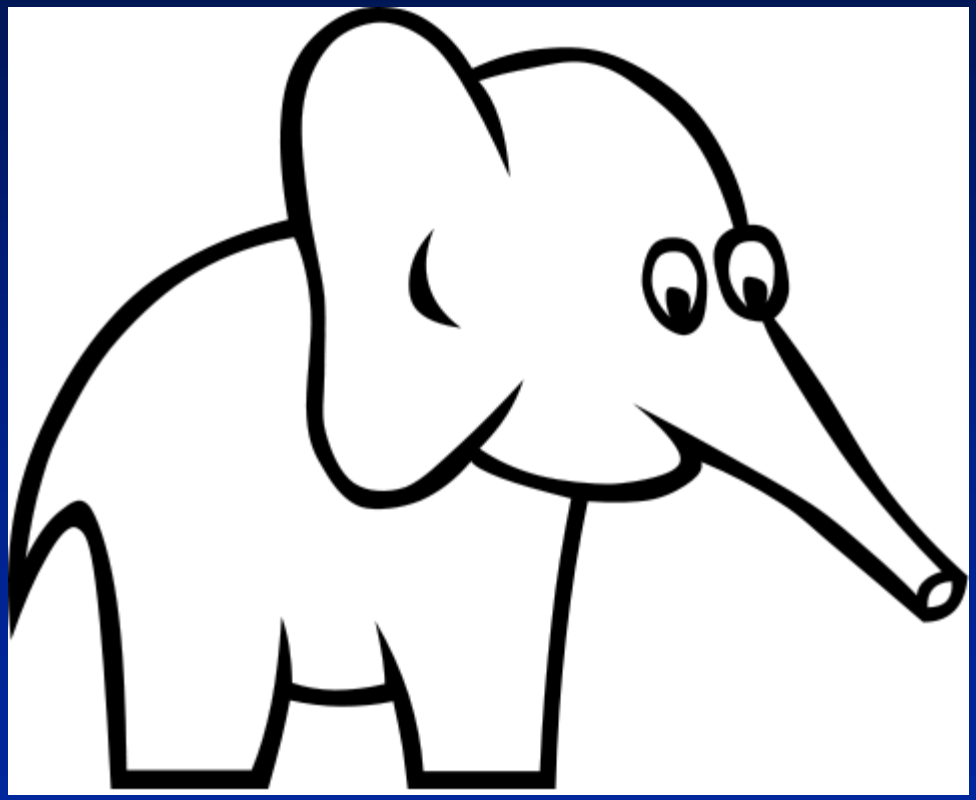
The Relationship between Antimicrobial Resistance and Patient Outcomes: Mortality, Length of Hospital Stay, and Health Care Costs

Sara E. Cosgrove
Division of Infectious Diseases, The Johns Hopkins Medical Institutions, Baltimore, Maryland

Elimizde kalanlar , Yeni (?) seçenekler

- **Kolistin**
- Tigesiklin
- Fosfomisin ?
- Kloramfenikol ?
- Aminoglikozid
- Kinolonlar

- Monoterapi?
- Kombinasyon?



Diagnostic Microbiology and Infectious Disease

Volume 75, Issue 4, April 2013, Pages 331–336

Review

Tigecycline: an update ☆

Gary E. Stein[a], Timothy Babinchak[b, 1]

Table 2.

Mortality by infection type (reproduced from Wyeth Pharmaceuticals Inc., 2012).

Infection type	Tigecycline		Comparator		Risk difference, % (95% CI)[a]
	n/*N*	%	*n*/*N*	%	
cSSSI	12/834	1.4	6/813	0.7	0.7 (−0.3 to 1.7)
cIAI	42/1382	3.0	31/1393	2.2	0.8 (−0.4 to 2.0)
CAP	12/424	2.8	11/422	2.6	0.2 (−2.0 to 2.4)
HAP	66/467	14.1	57/467	12.2	1.9 (−2.0 to 6.3)
Non-VAP[b]	41/336	12.2	42/345	12.2	0.0 (−4.9 to 4.9)
VAP[b]	25/131	19.1	15/122	12.3	6.8 (−2.1 to 15.7)
RP	11/128	8.6	2/43	4.7	3.9 (−4.0 to 11.9)
DFI	7/553	1.3	3/508	0.6	0.7 (−0.5 to 1.8)
Overall adjusted	150/3788	4.0	110/3646	3.0	0.6 (0.1 to 1.2)[c]

Tigesiklin

- Endikasyonlarında kullanalım (İntraabdominal, Deri Yumuşak doku)
- Kolistin + Tigesiklin kombinasyonları genellikle sinerjik değil
- Özellikle Ab için olumsuz deneyimler !
- Tigesikline direnç gelişimi hızlı
- Üçlü kombinasyonlarda yer alabilir?

Kolistin

- Karbapenem direncinde KOLİSTİN bir seçenek (tek seçenek)
- Klinik olarak olumlu veri var
- Dozun yüksek olması ve üç dozda verilmesi direnç gelişmesi açısından daha az riskli !
- Heterorezistans nedeniyle monoterapi riskli?

  (özellikle Ab için veri çok)

- Kolistin + Karbapenem(en sık kullanılan)
- Kolistin + Sulbaktam
- Kolistin + Sefepim veya Beta-laktam olumlu veriler !!!

Kolistin Kombinasyon

- **Kolistin + Rifampisin**

  -Nefrotoksisite

- **Kolistin + Aminoglikozid**

  -AG: Akciğerlere geçişi zayıf?

  -Nefrotoksisite

Kolistin

- Pnömonilerde inhalasyon tedavisi (?)
- Menenjitlerde intraventriküler/intratekal tedavi etkili
- Karaciğer yetmezliğinde doz ayarlamasına gerek yok
- Böbrek yetmezliğinde dozu ayarla
- Toksisite riski var!

Nefrotoksik ve nörotoksik !!!

Yükleme ve Yüksek Doz: Klinik Sonuç

300 mg yükleme – 2x150 mg idame

- **28 atak, 18 KDE ve 10 VİP**
- ***A.baumannii*(13), *K.pneumoniae*(13), *P.aeruginosa*(2)**
- **14 monoterapi, 14 kombinasyon (AG veya Karbapenem)**
- **Klinik kür: %82.1**
- **Akut böbrek hasarı %17.8**

Dalfino L et al. Clin Infect Dis 2012

Kolistini çok kullanmak?

NEFROTOKSİSİTE

Eski çalışmalar(1962-1977)
Genellikle IM verilmiş
Yüksek dozlar

%10.5-50(%20.2-%36)

- **Yeni çalışmalar**
- **Nefrotoksisite tanımında farklılıklar**
  Kolistin %14-18.6
- **Doza bağımlı, membran permeabilite artışı, akut tübüler nekroz**

Falagas ME et al. Critical Care 2006

- **NÖROTOKSİSİTE**
- **Eski çalışmalar**
  Parestezi %7.3-27
  Apne
  Nöromuskuler blok
- **Yeni çalışmalar**

Nörotoksisite yok ???

Kolistin Nefrotoksisite
Türkiye'den Deneyim

Scand J Infect Dis. 2014 Oct;46(10):678-85. doi: 10.3109/00365548.2014.926021. Epub 2014 Jul 30.

Colistin nephrotoxicity increases with age.

Balkan II[1], Dogan M, Durdu B, Batirel A, Hakyemez IN, Cetin B, Karabay O, Gonen I, Ozkan AS, Uzun S, Demirkol ME, Akbas S, Kacmaz AB, Aras S, Mert A, Tabak F.

Author information

Abstract

BACKGROUND: Colistin (COL) has become the backbone of the treatment of infections due to extensively drug-resistant (XDR) Gram-negative bacteria. The most common restriction to its use is acute kidney injury (AKI).

METHODS: We conducted a retrospective cohort study to evaluate risk factors for new-onset AKI in patients receiving COL. The cohort consisted of 198 adults admitted to 9 referral hospitals between January 2010 and October 2012 and treated with intravenous COL for ≥ 72 h. Patients with no pre-existing kidney dysfunction were compared in terms of risk factors and outcomes of AKI graded according to the RIFLE criteria. Logistic regression analysis was used to identify associated risk factors.

RESULTS: A total of 198 patients met the inclusion criteria, of whom 167 had no pre-existing kidney dysfunction; the mean patient age was 58.77 (± 18.98) y. Bloodstream infections (34.8%) and ventilator-associated pneumonia (32.3%) were the 2 most common indications for COL use. New-onset AKI developed in 46.1% of the patients, graded as risk (10%), injury (15%), and failure (21%). Patients with high Charlson co-morbidity index (CCI) scores ($p = 0.001$) and comparatively low initial glomerular filtration rate (GFR) estimations ($p < 0.001$) were more likely to develop AKI, but older age ($p = 0.001$; odds ratio 5.199, 95% confidence interval 2.684-10.072) was the major predictor in the multivariate analysis. In-hospital recovery from AKI occurred in 58.1%, within a median of 7 days.

CONCLUSIONS: COL-induced nephrotoxicity occurred significantly more often in patients older than 60 y of age and was related to low initial GFR estimations and high CCI scores, which were basically determined by age.

Kolistine Dirençli Bakteriler

- *Serratia* spp.
- *Proteus* spp.
- *Providencia* spp.
- *Burkholderia cepacia*
- *Morganella* spp.
- *Moraxella catarrhalis*

- Kolistine direnç !
- Heterorezistans A.baumannii (+)

Infection due to colistin-resistant *Enterobacteriacae* in critically-ill patients

Musa Abubakar Garbati[1], Aref Bin Abdulhak[2], Kamaldeen Baba[3], Hussam Sakkijha[4]

[1]*Section of Infectious Diseases, Department of Medicine, King Fahad Medical City, Riyadh, Saudi Arabia*
[2]*Internal Medicine Department,School of Medicine, University of Missouri-Kansas City, Kansas City, MO, USA.*
[3]*Department of Clinical Microbiology, King Fahad Medical City, Riyadh, Saudi Arabia*
[4]*Department of Pulmonary and Critical Care Medicine, King Fahad Medical City, Riyadh, Saudi Arabia*

J Infect Dev Ctries 2013; 7(10):713-719.doi:10.3855/jidc.2851

Eski/yeni çözüm?

Could chloramphenicol be used against ESKAPE pathogens? A review of *in vitro* data in the literature from the 21st century

February 2014, Vol. 12, No. 2 , Pages 249-264 (doi:10.1586/14787210.2014.878647)

The widespread use of antibiotics has been associated with the emergence of antimicrobial resistance among bacteria. 'ESKAPE' (*Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acintobacter baumannii, Pseudomonas aeruginosa* and *Enterobacter* spp.) pathogens play a major role in the rapidly changing scenario of antimicrobial resistance in the 21st century. Chloramphenicol is a broad spectrum antibiotic that was abandoned in developed countries due to its association with fatal aplastic anemia. However, it is still widely used in the developing world. In light of the emerging problem of multi-drug resistant pathogens, its role should be reassessed. Our paper reviews *in vitro* data on the activity of chloramphenicol against ESKAPE pathogens. Susceptibility patterns for Gram-positives were good, although less favorable for Gram-negatives. However, in combination with colistin, chloramphenicol was found to have synergistic activity. The risk-benefit related to chloramphenicol toxicity has not been analyzed. Therefore, extra precautions should be taken when prescribing this agent.

FOSFOMİSİN (IV)

31 çalışmanın gözden geçirilmesi…

- **Günlük doz 2-24 g/gün, 6-8 saatte bir**
- **5-21 gün**
- **Tek başına veya kombinasyon**
- **Klinik başarı %81.2**

Falagas ME et al. Clin Infect Dis 2008

Akılcı ?

- Riskleri ortadan kaldırmaya çalış !
- Kolonizasyonu tedavi etme
- Ampirik tedavide etkeni kapsa !
- Antibiyotik baskısı/direnç geliştirme ? Antibiyotikleri –zamanında- kes !

- Laboratuvar ile dinamik bir ilişki içinde !
- Doz, FK/FD ilişkilerini gözeterek !

Ampirik tedavi etkene uygun olmalı !

- “Kültür”lü bir dayanağı olan
- Tamamen lokal verilere dayanan
- Dinamik
- Sıkı işbirliği içinde uygulanan
- “Erken” başlanan ampirik tedavi

uygun ampirik tedavidir!!

Uygun ampirik tedavi

- Risklere göre ?
- Kolonizasyona göre?
- Laboratuvar destekli ?
  Hızlı tanı?
  Mekanizma ?

Predictive Models for Identification of Hospitalized Patients Harboring KPC-Producing Klebsiella pneumoniae

Mario Tumbarello, Enrico Maria Trecarichi, Fabio Tumietto, Valerio Del Bono, Francesco Giuseppe De Rosa, Matteo Bassetti, Angela Raffaella Losito, Sara Tedeschi, Carolina Saffioti, Silvia Corcione, Maddalena Giannella, Francesca Raffaelli, Nicole Pagani, Michele Bartoletti, Teresa Spanu, Anna Marchese, Roberto Cauda, Claudio Viscoli and Pierluigi Viale

***Antimicrob. Agents Chemother.* 2014, 58(6):3514. DOI:**

TABLE 2 Logistic regression analysis of risk factors for KPCKP strain isolation and for KPCKP infection

Variable[a]	OR (95% CI)	*P*
KPCKP isolation		
≥2 previous acute-care hospitalizations[b]	5.92 (4.40–7.98)	<0.001
Indwelling central venous catheter[c]	1.66 (1.29–2.12)	<0.001
Recent carbapenem therapy[d]	2.98 (2.19–4.05)	<0.001
Recent fluoroquinolone therapy[d]	1.69 (1.29–2.21)	<0.001
Previous intensive care unit admission[b]	5.13 (3.49–7.53)	<0.001
Indwelling urinary catheter[c]	3.89 (3.03–4.99)	<0.001
Hematological cancer	1.90 (1.27–2.83)	0.002
Surgical drain[c]	1.62 (1.16–2.45)	0.004
KPCKP infection		
≥2 previous acute-care hospitalizations[b]	4.26 (3.02–6.01)	<0.001
Indwelling central venous catheter[c]	2.59 (1.91–3.50)	<0.001
Recent carbapenem therapy[d]	3.59 (2.46–5.23)	<0.001
Recent fluoroquinolone therapy[d]	2.22 (1.59–3.10)	<0.001
Charlson score ≥3[c]	7.49 (5.46–10.27)	<0.001
Recent surgical procedures[d]	2.03 (1.48–2.76)	<0.001
Neutropenia[c]	3.19 (1.50–6.78)	0.003

Ampirik tedavi kolonizasyonla belirlenebilir mi?

- Kolonizasyon varlığı ?

VAP olgularında en az haftada iki solunum kültürü ile sürveyans etkeni saptamakta

% 70 duyarlı, % 80 spesifik?

Rektal kolonizasyon bakteriyemi ilişkisi???

(Risk gruplarında belirleyici faktör)

Surveillance Cultures Growing Carbapenem-Resistant *Acinetobacter baumannii* Predict the Development of Clinical Infections: A Retrospective Cohort Study

Rachel Latibeaudiere,[1] Rossana Rosa,[1] Panthipa Laowansiri,[1] Kristopher Arheart,[2,3] Nicholas Namias,[4] and L. Silvia Munoz-Price[5,6]

[1]Department of Medicine, [2]Department of Public Health Sciences, [3]Division of Statistics, and [4]Department of Surgery, University of Miami Miller School of Medicine, Florida; and [5]Institute for Health and Society, and [6]Department of Medicine, Medical College of Wisconsin, Milwaukee

Background. We aimed to determine the effect of the presence of carbapenem-resistant *Acinetobacter baumannii* in accordance with surveillance cultures on the subsequent development of clinical infections by this organism.

Methods. This retrospective cohort study was conducted at a tertiary hospital from January 2010 to November 2011. We included all consecutive patients admitted to the trauma intensive care unit, who had weekly surveillance cultures performed (from rectum, and if intubated, respiratory secretions), and without evidence of *A. baumannii* infections prior to the collection of the first surveillance culture. Univariable and multivariable analyses were performed using log-binomial regression. Survival analyses were performed using Cox proportional hazards.

Results. Three hundred sixty-four patients were included, of whom 49 (13.5%) had carbapenem-resistant *A. baumannii* on surveillance cultures. Patients with positive surveillance cultures had 8.4 (95% confidence interval [CI], 5.6–12.7; $P < .0001$) times the risk of developing a subsequent *A. baumannii* infection compared with patients who remained negative on surveillance cultures. Multivariable analysis showed significant associations between clinical infection and both positive surveillance cultures (relative risk [RR], 5.9 [95% CI, 3.8–9.3]; $P < .0001$) and mechanical ventilation (RR, 4.3 [95% CI, 1.03–18.2]; $P = .05$). On survival analyses, the only variable associated with the development of clinical infections was the presence of positive surveillance cultures (hazard ratio, 16.3 [95% CI, 9.1–29.1]; $P < .001$).

Conclusions. Presence of carbapenem-resistant *A. baumannii* on surveillance cultures is strongly associated with subsequent development of carbapenem-resistant *A. baumannii* infections. Prevention efforts should be focused at limiting the acquisition of this organism during hospitalization.

Keywords. *Acinetobacter baumannii*; carbapenem-resistant; surveillance cultures; clinical infections; intensive care unit.

Multidrug-resistant bacteria: what is the threat?

Matteo Bassetti[1] *and Elda Righi*[1]

[1]*Infectious Diseases Division, Santa Maria Misericordia University Hospital, Udine, Italy*

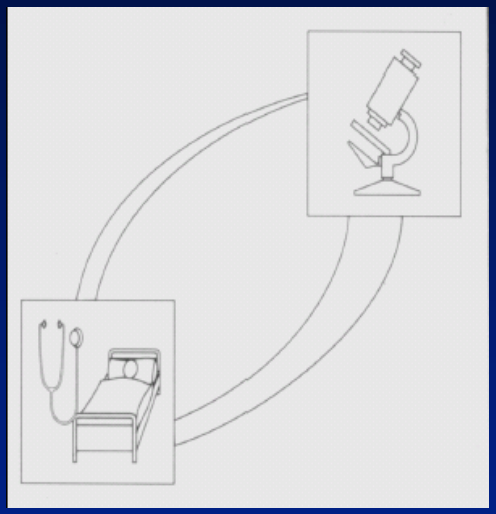
Table 3. Modification of the initial therapy due to colonization/previous infection with resistant bacteria

Resistant bacteria	Primary choice	Secondary choice
MRSA	Daptomycin or linezolid	Vancomycin
VRE	Daptomycin or linezolid	Tigecycline
ESBL	Meropenem	Ertapenem
Carbapenemase-producing Enterobacteriaceae	High-dose meropenem (6 g/d) + tigecycline + colistin	Tigecycline + gentamicin + colistin
MDR *P aeruginosa*	Piperacillin-tazobactam + amikacin	Piperacillin-tazobactam + colistin
MDR *Acinetobacter baumannii*	Colistin + rifampin	Tigecycline + colistin
Stenotrophomonas maltophilia	Trimetoprim-sulfamethoxazole	Quinolone or tigecycline

Ampirik tedavide laboratuvar !!!

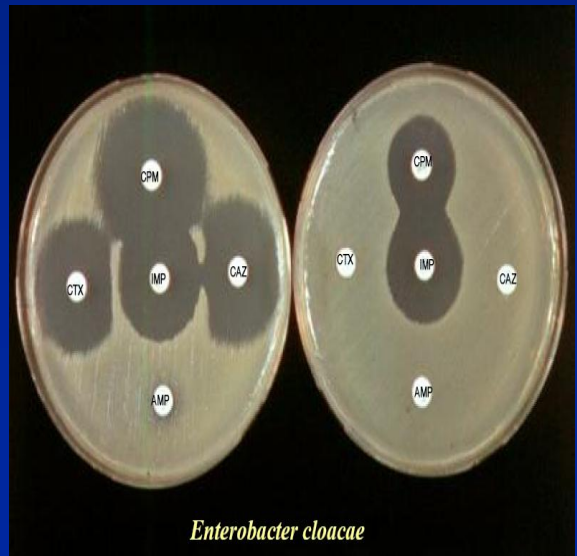
Acil Gram !

Moleküler hızlı tanı



Hızlı cins düzeyinde tanım

Standart antibiotik duyarlılığı



Karbapenem direncinde laboratuvar

Karbapenemaz ?

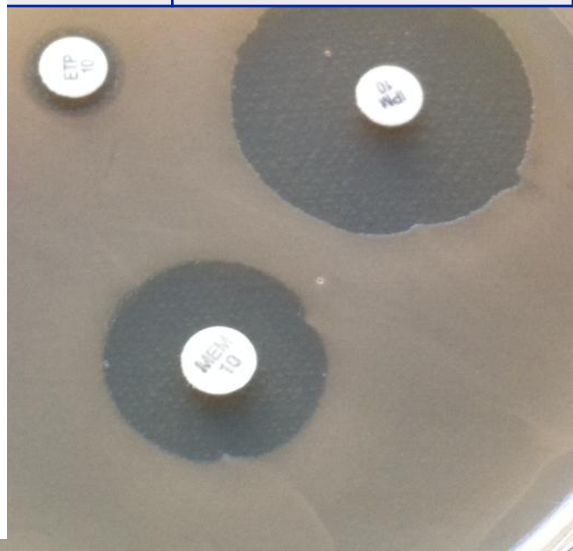
- **Hodge testi ? Gereksiz !**
- **IMP, MEM MİK değeri**
- **MEM ? İle tarama !**
- **MOLEKÜLER TANI**

Antibiyotik	Sonuç
Sefotaksim	**R**
Seftazidim	**R**
İmipenem	**S**
Ertapenem	**R**
Amikasin	**S**
Sefepim	**R**
Kolistin	**S ?**
Tigesiklin	**S ?**

Table 1. Clinical breakpoints and screening cut-off values for carbapenemase-producing Enterobacteriaceae (according to EUCAST methodology).

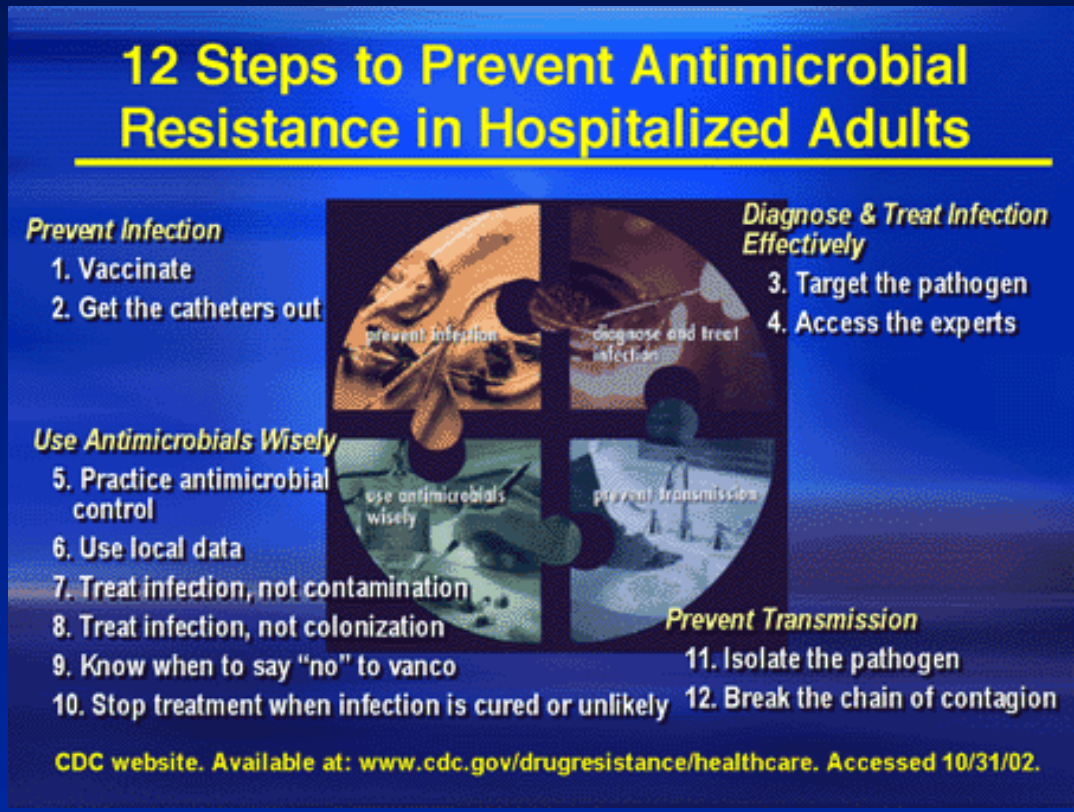
Carbapenem	MIC (mg/L)		Disk diffusion zone diameter (mm) with 10 µg disks	
	S/I breakpoint	Screening cut-off	S/I breakpoint	Screening cut-off
Meropenem[1]	≤2	>0.12	≥22	<25[2]
Imipenem[3]	≤2	>1	≥22	<23
Ertapenem[4]	≤0.5	>0.12	≥25	<25

[1]Best balance of sensitivity and specificity



Elimizdekileri en iyi kullanmak !

- FK/FD
- Kombinasyon
- Tedavi süresi



DOZ
(NP tedavi önerileri-IDSA)

Antibiyotik	Uygulama Önerisi
Sefepim	8-12 saatte bir 1-2 g
Seftazidim	8 saatte bir 2 g
İmipenem	6 saatte bir 500mg ya da 8 saatte bir 1g
Meropenem	8 saatte bir 1g
Piperasilin/Tazobaktam	6 saatte bir 4.5 g
Sefoperazon/Sulbaktam	12 saatte bir 2 g
Gentamisin*	7 mg/kg/gün (tek doz)
Tobramisin*	7 mg/kg/gün (tek doz)
Netilmisin*	7 mg/kg/gün (tek doz)
Amikasin*	20 mg/kg/gün (tek doz)
Levofloksasin	750 mg /gün
Siprofloksasin	8 saatte bir 400 mg
Vankomisin*	15 mg/kg her 12 saatte bir
Linezolid	12 saatte bir 600 mg

* Etkinlik ve yan etki yönünden serum düzeyleri ile izlenmesi önerilmektedir.

Farmakokinetik

Table 1
Summary of design and results for clinical studies of prolonged infusion (PI) of β-lactams.

Reference	Study design	Patients	Infection	Dosing regimen	PI findings
Arnold et al., 2013 [36]	Retrospective, single centre	503, ICU	Gram-negative bacteria	FEP or TZP or MEM 3-h inf. vs. FEP or TZP or MEM 30-min inf.	No difference in treatment success rates or mortality
Bauer et al., 2013 [37]	Retrospective, single centre	87, bacteraemia or pneumonia	*Pseudomonas aeruginosa*	FEP 2 g q8h 4-h inf. vs. FEP 2 g q8h 30-min inf.	Significantly lower mortality (20% vs. 3%)
Chastre et al., 2008 [20]	Prospective, multicentre, randomised	531, VAP	Gram-positive and -negative bacteria	DOR 500 mg q8h 4-h inf. vs. IMI 500 mg q6h 30-min inf. or IMI 1 g q8h 1-h inf.	Comparable clinical (68.3% vs. 64.8%) and microbiological (73.3% vs. 67.3%) cure rates; no difference in mortality (10.8% vs. 9.5%)
Dow et al., 2011 [29]	Retrospective, single centre	121, ICU	Gram-negative bacteria	TZP 3.375 g q8h or MEM 500 mg q6h 3- or 4-h inf. vs. TZP 3.375 g q6h or MEM 500 mg q6h 30-min inf.	No difference in mortality (12.4% vs. 20.7%)
Esterly et al., 2012 [32]	Retrospective, single centre	71, bacteraemia	*Actnetobacter baumannit*, *P. aeruginosa*, Enterobacteriaceae	IMI or MEM 3-h inf. vs. IMI or MEM 30-min inf.	No difference in mortality (28.6% vs. 24.1%)
Falagas et al., 2013 [38]	Meta-analysis, multicentre	1229, mixed infections	Gram-positive and -negative bacteria	TZP or IMI or MEM CI or EI vs. TZP or IMI or MEM 20–60-min inf.	Significantly lower mortality (RR = 0.59)
Itabashi, 2007 [28]	Prospective, single centre	42, severe pneumonia	Gram-positive and -negative bacteria	MEM 500 mg q12h 4-h inf. vs. MEM 500 mg q12h 1-h inf.	Significantly lower mortality (5.6% vs. 37.5%)
			ria	DOR 1 g q8h 4-h inf. × 7 days vs. IMI 1 g q8h 1-h inf. × 10 days	Clinical cure (45.6% vs. 56.8%) numerically lower and 28-day mortality numerically higher (21.5% vs. 14.8%) in DOR treatment arm
			ria	TZP 3.375 g q8h 4-h inf. vs. TZP 2.25–4.5 g q6–8 h 30-min inf.	Significantly lower 30-day mortality (19% vs. 38%)
				TZP 3.375 g q8h 4-h inf. vs. TZP 3.375 g q4h or q6h 30-min inf.	Significantly lower mortality (12.2% vs. 31.6%) in severely ill

International Journal of Antimicrobial Agents 43 (2014) 105–113

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journal homepage: http://www.elsevier.com/locate/ijantimicag

Review

Prolonging β-lactam infusion: A review of the rationale and evidence, and guidance for implementation

Shawn H. MacVane[a], Joseph L. Kuti[a], David P. Nicolau[a,b,*]

KPC(+) *K. pneumoniae* -Tedavi

41 bakteriyemi

- 28 günlük mortalite %39
- Kombinasyon – mortalite 2/15(%13.3)
- Monoterapi – mortalite 11/19(%57.8), p=0.01

- En sık kombinasyon
  -Karbapenem + Kolistin
  -Karbapenem + Tigesiklin

- Kombinasyon tedavisi(kesin tedavi olarak) yaşamın devamı açısından bağımsız koruyucu faktör (OR 0.07, p=0.02)

Qureshi Z et al. Antimicrob Agents Chemother 2010

Carbapenemase-Producing Klebsiella pneumoniae Bloodstream Infections: Lowering Mortality by Antibiotic Combination Schemes and the Role of Carbapenems

George L. Daikos, Sophia Tsaousi, Leonidas S. Tzouvelekis, Ioannis Anyfantis, Mina Psichogiou, Athina Argyropoulou, Ioanna Stefanou, Vana Sypsa, Vivi Miriagou, Martha Nepka, Sarah Georgiadou, Antonis Markogiannakis, Dimitris Goukos and Athanasios Skoutelis

Antimicrob. Agents Chemother. 2014. 58(4):2322. DOI:

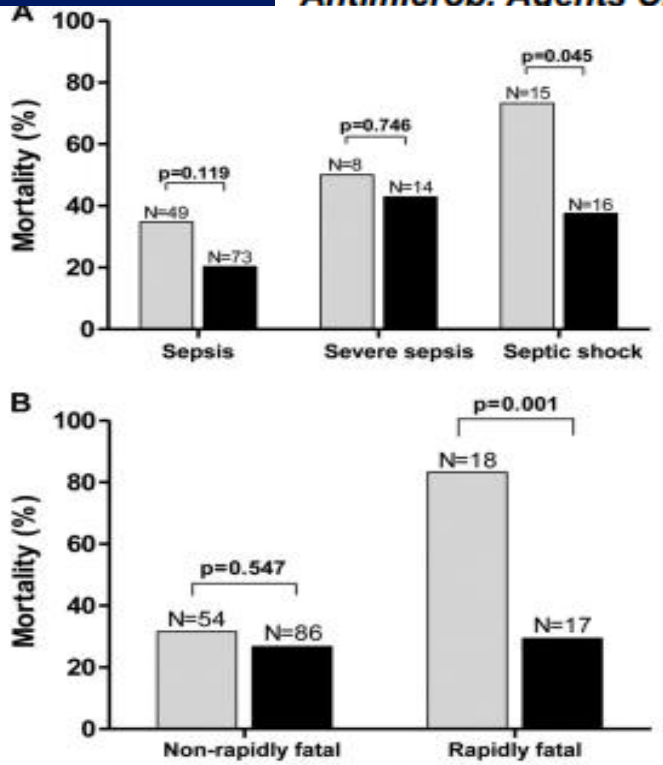


FIG 2 Graphic presentation of the effect of treatment (monotherapy [gray bars] versus combination therapy [black bars]) by severity of underlying disease (A) and by severity of sepsis (B). Numbers above columns indicate the number of patients.

TABLE 2 Outcome of patients with carbapenemase-producing *K. pneumoniae* bloodstream infections according to treatment regimen

Antimicrobial regimen	No. of patients			Mortality, %
	Total	Survived	Died	
Combination therapy	103	75	28	27.2
Carbapenem-containing regimen	31	25	6	19.3
Carbapenem + tigecycline + aminoglycoside or colistin		11	0	
Carbapenem + tigecycline		2	2	
Carbapenem + aminoglycoside		8	1	
Carbapenem + colistin		4	3	
Carbapenem-sparing regimen	72	50	22	30.6
Tigecycline + aminoglycoside + colistin		8	3	
Tigecycline + aminoglycoside		11	9	
Tigecycline + colistin		16	5	
Aminoglycoside + colistin		12	5	
Other		3	0	
Monotherapy	72	40	32	44.4
Tigecycline		16	11	
Colistin		10	12	
Aminoglycoside		7	2	
Carbapenem		5	7	
Other		2	0	
No active agent	12[a]	8	4	33.3

[a] Eight patients were infected with panresistant *Klebsiella pneumoniae*.

Clinical Microbiology Reviews

Carbapenemases in Klebsiella pneumoniae and Other Enterobacteriaceae: an Evolving Crisis of Global Dimensions

L. S. Tzouvelekis, A. Markogiannakis, M. Psichogiou, P. T. Tassios and G. L. Daikos

Clin. Microbiol. Rev. 2012, 25(4):682. DOI: 10.1128/CMR.05035-11.

TABLE 5 Results of carbapenem monotherapy in 50 CPE-infected patients from 15 studies[a]

MIC of carbapenem (μg/ml)	No. of patients	No. of successes	No. of failures	% Failure
≤1	17	12	5	29.4
2	12	9	3	25.0
4	7	5	2	28.6
8	6	4	2	33.3
Subtotal	42	30	12	28.6[b]
>8	8	2	6	75.0[b]
Total	50	32	18	36

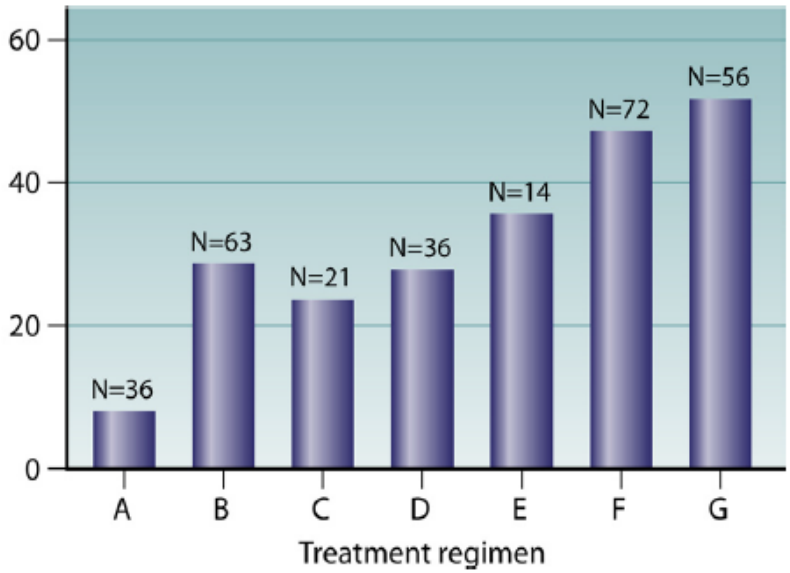


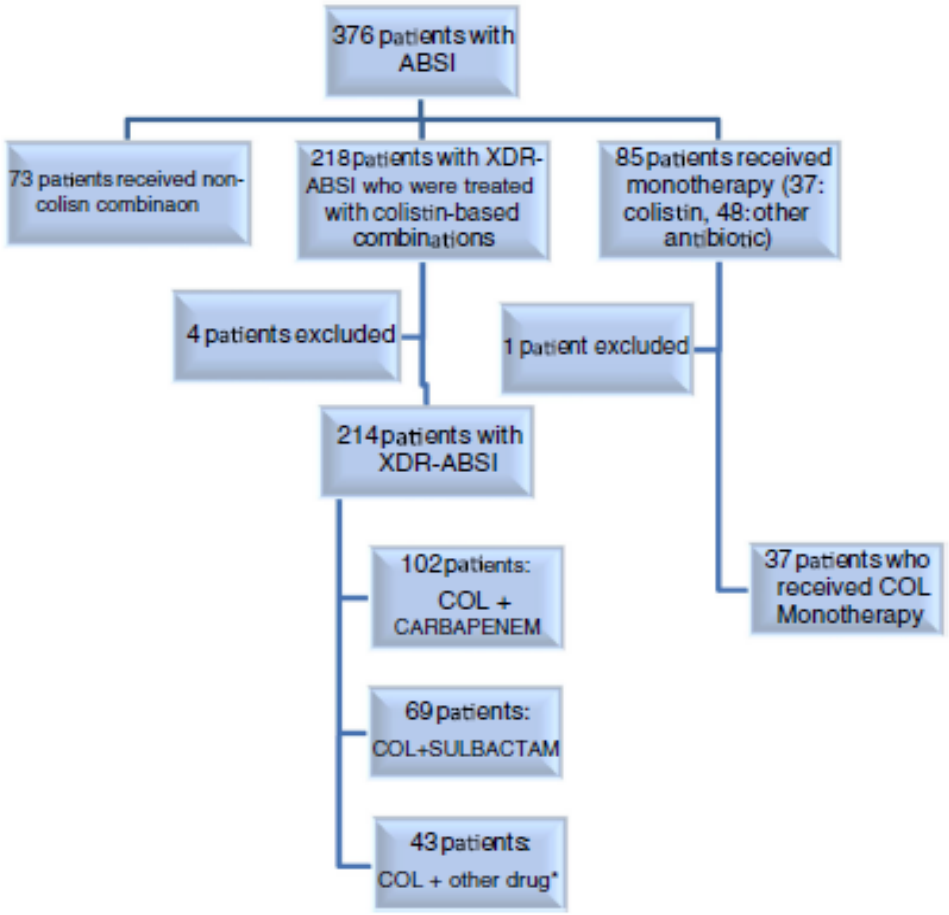
FIG 2 Outcomes of infections caused by carbapenemase-producing *Klebsiell pneumoniae*, according to treatment regimen. Regimen A, combination ther apy with ≥2 active drugs, one of which was a carbapenem; regimen B, combi nation therapy with ≥2 active drugs, not including a carbapenem; regimen C monotherapy with an aminoglycoside; regimen D, monotherapy with a car bapenem; regimen E, monotherapy with tigecycline; regimen F, monotherap

Eur J Clin Microbiol Infect Dis (2014) 33:1311–1322
DOI 10.1007/s10096-014-2070-6

ARTICLE

Comparison of colistin–carbapenem, colistin–sulbactam, and colistin plus other antibacterial agents for the treatment of extremely drug-resistant *Acinetobacter baumannii* bloodstream infections

A. Batirel · I. I. Balkan · O. Karabay · C. Agalar · S. Akalin · O. Alici · E. Alp · F. A. Altay · N. Altin · F. Arslan · T. Aslan · N. Bekiroglu · S. Cesur · A. D. Celik · M. Dogan · B. Durdu · F. Duygu · A. Engin · D. O. Engin · I. Gonen · E. Guclu · T. Guven · C. A. Hatipoglu · S. Hosoglu · M. K. Karahocagil · A. U. Kilic · B. Ormen · D. Ozdemir · S. Ozer · N. Oztoprak · N. Sezak · V. Turhan · N. Turker · H. Yilmaz



Characteristic/variable	Colistin combination group, *n* (%)	Colistin monotherapy group, *n* (%)	*p*-Value
Total (*n*)	214	36	
Age (mean ± SD) (years)	59.1±19.6	58.3±20.5	0.81
Gender (male)	141 (65)	21 (58)	0.46
Hospital stay prior to XDR-ABSI (mean ± SD, days)	23.9±21.9	22.3±19.9	0.69
ICU stay prior to XDR-ABSI (mean ± SD, days)	19.1±19.3	18.9±20.8	0.96
Pitt bacteremia score (mean ± SD)	7.1±3.6	6.8±2.9	0.62
APACHE II score[a] (mean ± SD)	18.6±6.9	17.9±7.1	0.82
Charlson comorbidity index (mean ± SD)	3.3±2.2	3.5±2.2	0.55
Concomitant other infection	128 (59)	20 (56)	0.63
Initiation of effective therapy			0.13
Early (within 24 h)	152 (71)	21 (58.3)	
Late (after 24 h)	62 (29)	15 (41.7)	
Nephrotoxicity	36 (21.8)	9 (25)	0.88
Neurotoxicity[b]			
Present	3 (1.4)	0 (0)	
Unconscious/pharmacologic sedation	211 (98.6)	36 (100)	
Clinical outcome			0.19
Complete response/cure	99 (46.3)	11 (30.6)	
Partial response/improvement	68 (31.8)	16 (44.4)	
No response/failure	47 (22)	9 (25)	
Microbiologic outcome			0.001
Eradication present	171 (79.9)	20 (55.6)	
Redundant	43 (20.1)	16 (44.4)	
14-day survival	146 (68.2)	20 (55.5)	0.14
In-hospital crude mortality	112 (52.3)	26 (72.2)	0.03

Characteristic/variable	Colistin–carbapenem group, *n* (%)	Colistin–sulbactam group, *n* (%)	Colistin plus other agent group, *n* (%)	*p*-Value
Total, *n*	78	43	31	
Clinical outcome				0.93
Complete response/cure	40 (51.3)	25 (58.1)	12 (38.7)	
Partial response/improvement	22 (28.2)	8 (18.6)	12 (38.7)	
No response/failure	16 (20.5)	10 (23.3)	7 (22.6)	
Microbiologic outcome				0.48
Eradication present	64 (82)	38 (88.4)	27 (87)	
Redundant	14 (17.9)	5 (11.6)	4 (12.9)	
14-day survival	55 (70.5)	29 (67.4)	17 (54.8)	0.49
In-hospital crude mortality	38 (48.7)	19 (44.2)	19 (61.3)	0.33

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journal homepage: www.elsevier.com/locate/ijid

Blood stream infections due to OXA-48-like carbapenemase-producing *Enterobacteriaceae*: treatment and survival

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Table 4

Treatment outcomes

	Total (n = 36)	Survivors (n = 18)	Non-survivors (n = 18)	p-Value[a]
Time to active treatment, days, mean ± SD	1.25 ± 1.32	0.72 ± 1.18	1.78 ± 1.26	0.014
Duration of treatment, days, mean ± SD	14.58 ± 16.015	22.72 ± 18.68	6.44 ± 6.21	0.002[b]
Treatment modalities				
Colistin dual combination (n = 12)	12 (33.3)	5 (27.7)	7 (38.8)	0.725
Colistin triple combination (n = 12)	12 (33.3)	9 (50)	3 (16.6)	0.075
Non-colistin based combinations (n = 7)	7 (19.4)	1 (5.5)	6 (33.3)	0.018
Carbapenem monotherapy (n = 5)	5 (13.8)	3 (16.6)	2 (11.1)	1

[a] Univariate analysis.

[b] Duration of treatment is naturally longer in survivors.

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J Antimicrob Chemother
doi:10.1093/jac/dku168

Journal of Antimicrobial Chemotherapy

Combination therapy for carbapenem-resistant Gram-negative bacteria

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Carbapenem-resistant Gram-negative bacteria (CR-GNB) represent an increasing hazard in healthcare settings. A central question concerning the treatment of invasive infections caused by CR-GNB involves the use of combination therapy. Potential advantages of combination therapy include improved efficacy due to synergy, while the disadvantages include adverse events and increased antibiotic use with a potential drive towards resistance. Several observational studies have examined whether combination therapy offers an advantage over colistin/polymyxin monotherapy. We highlight the inherent limitations of these studies related to their observational design and sample size to show why they do not at present provide an answer to the question of combination versus monotherapy. This distinction is important to guide clinical practice until solid evidence has been obtained and to enable the recruitment of patients into randomized controlled trials. A few randomized controlled trials examining specific combinations have recently been completed or are ongoing. Currently, however, there is no evidence-based support for most combination therapies against CR-GNB, including colistin/carbapenem combination therapy.

Değişik Kombinasyonlar

Clinical Experience of Colistin-Glycopeptide Combination in Critically Ill Patients Infected with Gram-Negative Bacteria

Nicola Petrosillo,[a] Maddalena Giannella,[a] Massimo Antonelli,[b] Mario Antonini,[c] Bruno Barsic,[d] Laura Belancic,[d] Cagkan Inkaya A.,[e] Gennaro De Pascale,[b] Elisabetta Grilli,[a] Mario Tumbarello,[f] Murat Akova[e]

2nd Division of Infectious Diseases[a] and Department of Intensive Care Unit and Anaesthesia,[c] National Institute for Infectious Diseases Lazzaro Spallanzani, Rome, Italy; Department of Intensive Care and Anesthesiology[b] and Institute of Infectious Diseases,[f] Università Cattolica del Sacro Cuore, Rome, Italy; School of Medicine, University of Zagreb, Hospital for Infectious Diseases, Zagreb, Croatia[d]; Department of Medicine, Section of Infectious Diseases, Hacettepe University School of Medicine, Ankara, Turkey[e]

A colistin-glycopeptide combination (CGC) has been shown *in vitro* to be synergistic against multidrug-resistant Gram-negative bacteria (MDR GNB), especially *Acinetobacter baumannii*, and to prevent further resistance. However, clinical data are lacking. We carried out a retrospective multicenter study of patients hospitalized in intensive care units (ICUs) who received colistin for GNB infection over a 1-year period, to assess the rates of nephrotoxicity and 30-day mortality after treatment onset among patients treated with and without CGC for ≥48 h. Of the 184 patients treated with colistin, GNB infection was documented for 166. The main causative agents were MDR *A. baumannii* (59.6%), MDR *Pseudomonas aeruginosa* (18.7%), and carbapenem-resistant *Klebsiella pneumoniae* (14.5%); in 16.9% of patients, a Gram-positive bacterium (GPB) coinfection was documented. Overall, 68 patients (40.9%) received CGC. Comparison of patients treated with and without CGC showed significant differences for respiratory failure (39.7% versus 58.2%), ventilator-associated pneumonia (54.4% versus 71.4%), MDR *A. baumannii* infection (70.6% versus 52%), and GPB coinfection (41.2% versus 0%); there were no differences for nephrotoxicity (11.8% versus 13.3%) and 30-day mortality (33.8% versus 29.6%). Cox analysis performed on patients who survived for ≥5 days after treatment onset showed that the Charlson index (hazard ratio [HR], 1.26; 95% confidence interval [CI], 1.01 to 1.44; $P = 0.001$) and MDR *A. baumannii* infection (HR, 2.51; 95% CI, 1.23 to 5.12; $P = 0.01$) were independent predictors of 30-day mortality, whereas receiving CGC for ≥5 days was a protective factor (HR, 0.42; 95% CI, 0.19 to 0.93; $P = 0.03$). We found that CGC was not associated with higher nephrotoxicity and was a protective factor for mortality if administered for ≥5 days.

Değişik kombinasyonlar

JournalsASM.org

Effectiveness of a Double-Carbapenem Regimen for Infections in Humans Due to Carbapenemase-Producing Pandrug-Resistant *Klebsiella pneumoniae*

Helen Giamarellou, Lambrini Galani, Fotini Baziaka, Ilias Karaiskos

6th Department of Internal Medicine, Hygeia General Hospital, Athens, Greece

Ertapenem plus doripenem or meropenem were given in three patients suffering from pandrug-resistant, KPC-2-positive *Klebsiella pneumoniae* bacteremia (2 patients) and urinary tract infection (1 patient), respectively. All responded successfully, without relapse at follow-up. The results obtained should probably be attributed to ertapenem's increased affinity for the carbapenemases hindering doripenem/meropenem degradation in the environment of the microorganism.

- **February 2014 Antimicrobial Agents and Chemotherapy p. 851–858**

AAC
JournalsASM.org

LETTER TO THE EDITOR

Successful Ertapenem-Doripenem Combination Treatment of Bacteremic Ventilator-Associated Pneumonia Due to Colistin-Resistant KPC-Producing *Klebsiella pneumoniae*

Giancarlo Ceccarelli,[a] Marco Falcone,[b] Alessandra Giordano,[a] Maria Lina Mezzatesta,[c] Carla Caio,[c] Stefania Stefani,[c] Mario Venditti[a]

Department of Public Health and Infectious Diseases, Policlinico Umberto I, University of Rome Sapienza, Rome, Italy[a]; Department of Emergency Medicine, Policlinico Umberto I, University of Rome Sapienza, Rome, Italy[b]; Department of Bio-Medical Sciences, University of Catania, Catania, Italy[c]

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Oral Gentamicin Gut Decontamination for Prevention of KPC-Producing *Klebsiella pneumoniae* Infections: Relevance of Concomitant Systemic Antibiotic Therapy

Carlo Tascini,[a] Francesco Sbrana,[b] Sarah Flammini,[a] Enrico Tagliaferri,[a] Fabio Arena,[c] Alessandro Leonildi,[a] Ilaria Ciullo,[a] Francesco Amadori,[a] Antonello Di Paolo,[d] Andrea Ripoli,[b] Russell Lewis,[e] Gian Maria Rossolini,[c,f,g] Francesco Menichetti,[a] the GE Study Group

TABLE 1 Patient characteristics and clinical outcomes for decontaminated patients versus persistent carriers

Characteristic	Value for: Decontaminated patients (n = 34)	Persistent carriers (n = 16)	P value
No. (%) male	23 (68)	12 (75)	0.843
Mean age, yr, ± SD	66 ± 11	59 ± 15	0.141
No. (%) of ICU patients	2 (6)	8 (50)	0.001
Median (range) duration of treatment, days	9 (7–15)	21 (15–30)	<0.001
No. (%) with KPC-Kp infection[a]	5/34 (15)	12/16 (73)	<0.001
No. (%) died[a]	10/34 (29)	5/16 (31)	0.843

[a] In the 6-month follow-up period.

TABLE 4 Multivariate logistic regression for gut decontamination event

Predictor	Odds ratio	95% Confidence interval for odds ratio	P value
CSAT[a]	0.105	0.005–0.801	0.048
KPC-Kp infection[a]	0.139	0.021–0.754	<0.001
ICU stay	0.132	0.011–0.992	0.066

[a] Significant predictor.

Antimicrob. Agents Chemother. 2014, 58(4):1972.

Tedavi süreleri

? ? ? ? ?

Clinical management of infections caused by multidrug-resistant *Enterobacteriaceae*

Mercedes Delgado-Valverde, Jesús Sojo-Dorado, Álvaro Pascual and Jesús Rodríguez-Baño

Ther Adv Infect Dis
(2013) 1(2) 49–69
DOI: 10.1177/2049936113476284

Mechanism of resistance	Antimicrobial	Comment
ESBL and plasmid AmpC producers	Carbapenems	Drugs of choice for severe infections
	β-lactam/β-lactam inhibitors	ESBL: alternative to carbapenems if active *in vitro*. Data available mainly for urinary bacteremia due to *Escherichia coli*. AmpCs are not inhibited
	Cephalosporins	ESBL: potentially active for isolates with low MIC. Controversial AmpC: cefepime might be useful
	Temocillin	Potentially useful as definitive therapy
	Fluoroquinolones	Useful if *in vitro* active. Caution in case of isolates showing borderline MIC
	Aminoglycosides	Useful if active mainly for urinary tract infections
	Fosfomycin	Useful for cystitis
KPC, MLB, and OXA producers	Carbapenem	Potentially useful for isolates with low MIC (optimized dose). Probably worse than combination
	Aztreonam, cephalosporins	Aztreonam only for MLB or OXA-48 (without ESBL). Cephalosporins only for OXA-48 without ESBL. Potentially useful. Limited experience
	Colistin	Real efficacy is controversial. Optimized dosing might improve results
	Fosfomycin	Limited experience. To be used in combination
	Tigecycline	Limited experience. To be used in combination. Less efficacy expected in UTI
	Combinations	Better results in observational studies. Carbapenems should probably be included. A third drug may improve the results

ESBL, extended-spectrum β-lactamase; KPC, *Klebsiella pneumoniae* carbapenemase; MIC, minimum inhibitory concentration; MLB, metallo β-lactamase; OXA, oxacillinase; UTI, urinary tract infection.

GSBL: “Sonun Başlangıcı”

CLINICAL MICROBIOLOGY REVIEWS, Oct. 2005, p. 657–686
0893-8512/05/$08.00+0 doi:10.1128/CMR.18.4.657–686.2005

Vol. 18, No. 4

Extended-Spectrum β-Lactamases: a Clinical Update

David L. Paterson[1]* and Robert A. Bonomo[2]

Infectious Disease Division, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania,[1] and Infectious Disease Division, Louis Stokes VA Medical Center, Cleveland, Ohio[2]

- **GSBL algımızda değişim !!**
- **GSBL tedavisinde karbapenem dışında yaklaşım!**
- **CTX-M ..CAZ bir seçenek!?**
- **CLSI;EUCAST yeni önerilerinin klinik yansıması?**
- **Elimizdekileri koruyabilmek..**

TABLE 3. Recommended treatment for infections with ESBL-producing organisms

Infection type	Therapy of choice	Second-line therapy
Urinary tract infection	Quinolone[a]	Amoxicillin/clavualante
Bacteremia	Carbapenem	Quinolone[a]
Hospital-acquired pneumonia	Carbapenem	Quinolone[a]
Intra-abdominal infection	Carbapenem	Quinolone[a] (plus metronidazole)
Meningitis	Meropenem	Intrathecal polymyxin B

[a] If the organism is quinolone susceptible.

Tedavide seçenekler

	KAR	TZP	SEF	SCF
Antips	+	++	+	++
Anti Ab	++	-	+	++
ESBL	+++	+?	+?	+?
İBL	++	-	+	-
Direnç gelişimine etki	+++	-/+	+++	?

Ertapenem ?

Kinolon???

Gelecek Çözüm-1

- Yeni antibiyotikler ???

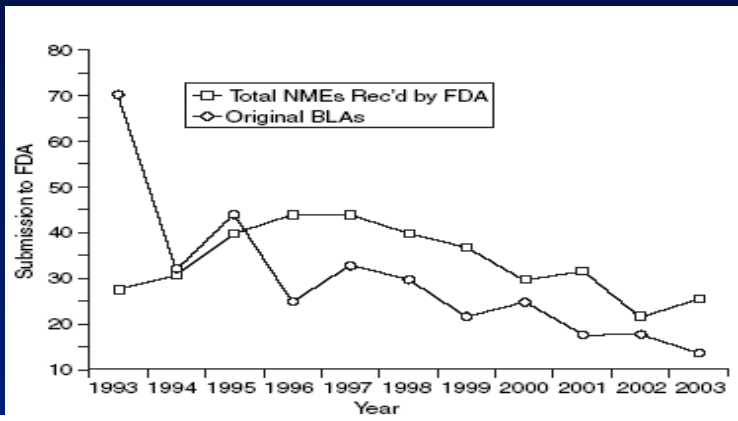


TABLE 8 Experimental β-lactamase inhibitors active against carbapenemases from *Enterobacteriaceae*

Inhibitor	Compound type	Inhibition spectrum (β-lactamase classes)	Susceptible carbapenemases[a]
BLI-489	Penem	A, C, D	KPC type
J-110,411 and J-111,225	1-β-Methyl carbapenem	A, C, B	IMP type
Mercaptomethyl sulfones	C-6-substituted penicillin sulfone	B	VIM and IMP types
2,3-(*S*,*S*)-Disubstituted succinic acids	Succinic acid	B	IMP type
Thiomandelic acids	Thiol	B	VIM and IMP types
Avibactam (NLX104)	Diazabicyclo-octanone	A, C, D	KPC type

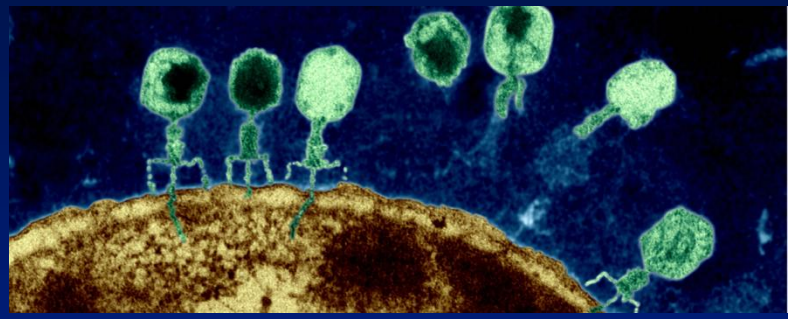
[a] Only carbapenemase types with documented susceptibility to the respective inhibitor are included.

TABLE 7 Experimental antimicrobial agents active against carbapenemase-producing *Enterobacteriaceae*

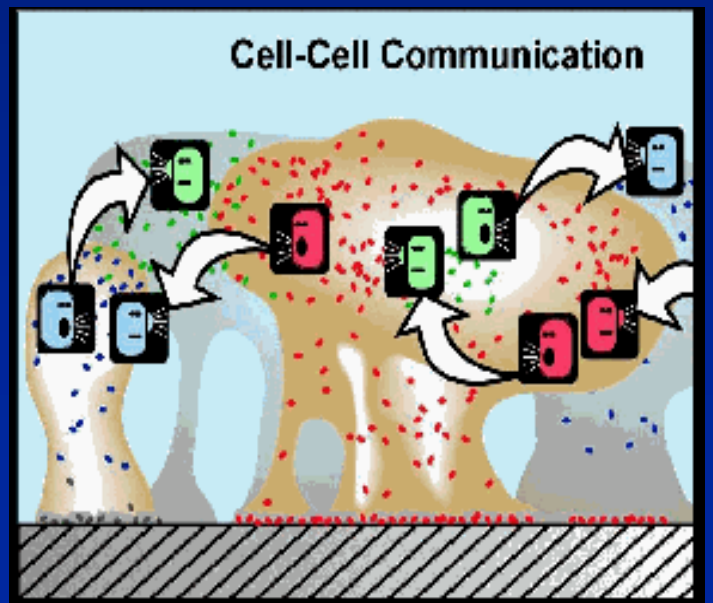
Drug	Compound type	Relevant target
BAL30072	Siderophore-containing sulfactam	*Enterobacteriaceae*, including MβL producers
Plazomicin (ACHN-490)	Sisomicin derivative	Gram-negative organisms, including carbapenemase producers
GSK2251052	Leucyl-tRNA synthetase inhibitor	Gram-negative organisms, including carbapenemase producers

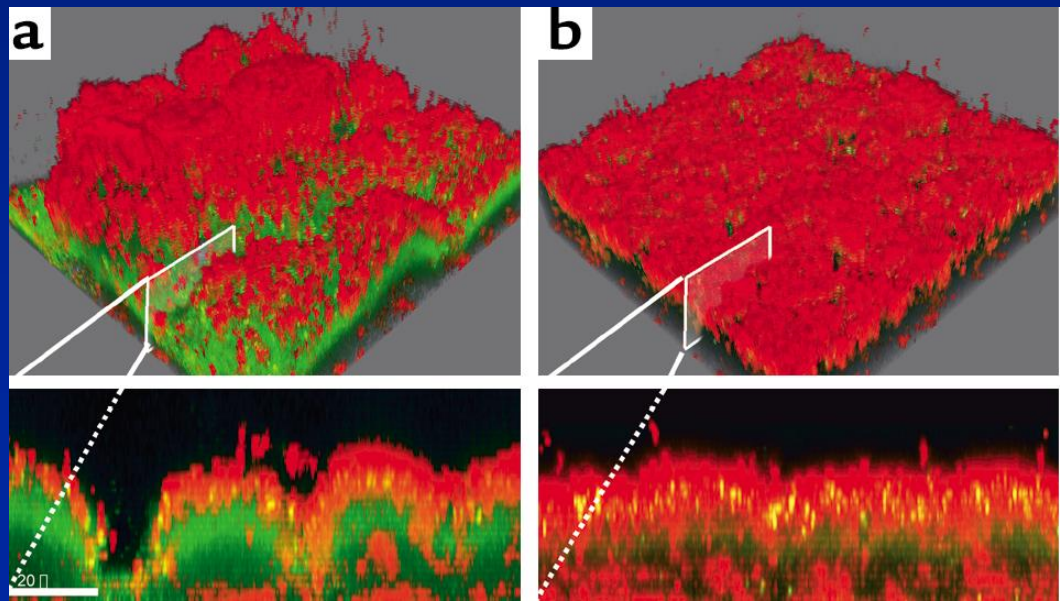
Gelecek çözüm-2

- Farklı tedavi yaklaşımları (FAJ ?)



- Mikroplarla “seviyeli ilişki” (iletişim)





Gelecek çözüm-3

- Aşı

International Journal of Antimicrobial Agents 32S (2008) S71–S78

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journal homepage: http://www.elsevier.com/locate/ijantimicag

Vaccination and passive immunisation against *Staphylococcus aureus*☆

Adam C. Schaffer, Jean C. Lee*

REVIEW

Arch. Immunol. Ther. Exp., 2006, 54, 113–120
PL ISSN 0004-069X

DOI 10.1007/s00005-

Novel therapies of multidrug-resistant *Pseudomonas aeruginosa* and *Acinetobacter* spp. infections: the state of the art

Marta Wróblewska

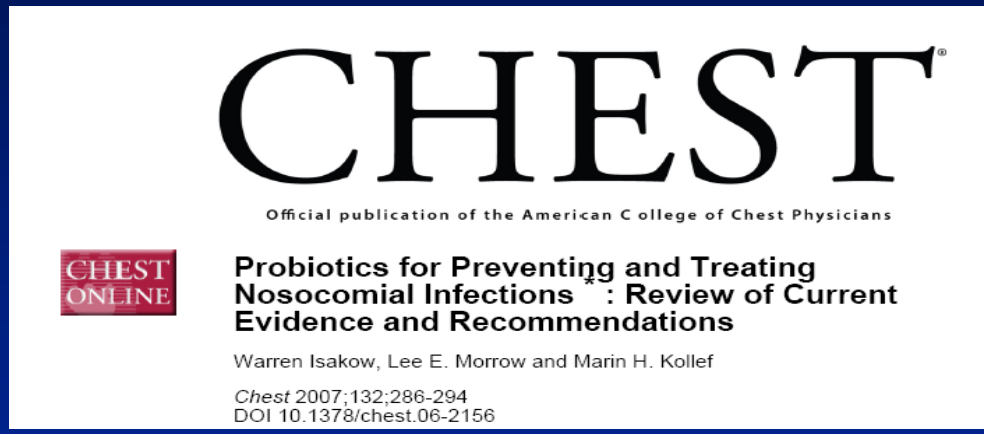
Table 2. Novel approaches to vaccine development against *P. aeruginosa* (based on Ramsey and Wozniak [67])

Target	Vaccine
Adherence inhibition	flagellin-based chimeric exotoxin A-pilus protein outer membrane protein (e.g. OprF) O-polysaccharide-toxin A conjugate
Type III secretion-translocation system inhibition	V antigen
Mucoid exopolysaccharide (alginate) inhibition	mucoid exopolysaccharide-alginate conjugate vaccine

Gelecek çözüm-4

- Koruyucu mikroplar
- A- insanda

Mikrobiom transferi!


CHEST

Official publication of the American College of Chest Physicians

CHEST ONLINE

Probiotics for Preventing and Treating Nosocomial Infections*: Review of Current Evidence and Recommendations

Warren Isakow, Lee E. Morrow and Marin H. Kollef

Chest 2007;132;286-294
DOI 10.1378/chest.06-2156

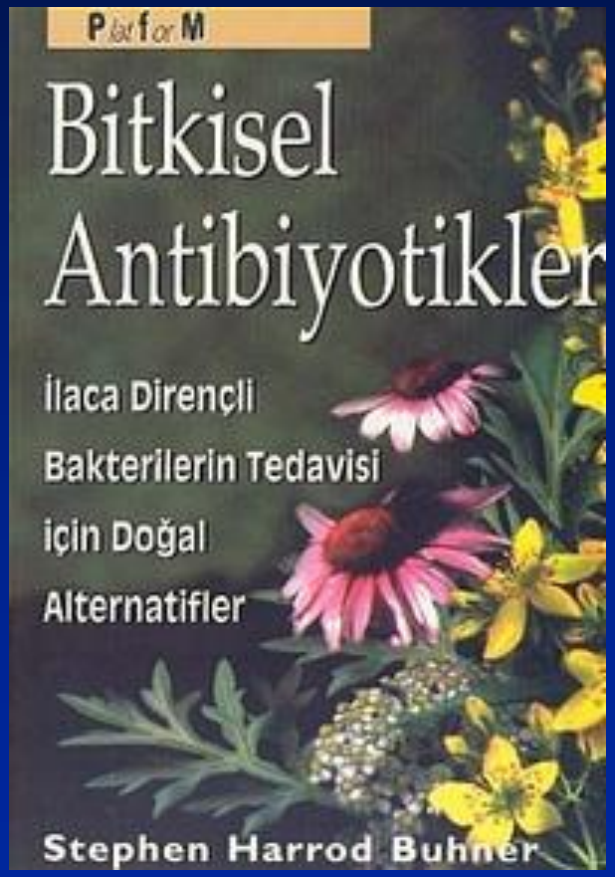
- B-Çevrede

"... Some have talked about spraying hospital rooms with susceptible commensal organisms to replace and compete with the disease agents."

Levy, 1997

Gelecek çözüm-5

? ? ?? ? ?



Çoklu Dirençli GNÇ İnfeksiyonlarının Akılcı Tedavisi SONUÇ!

SONUÇ

- Yakın gelecekte yeni antibiyotik beklenmiyor
- Laboratuvar, PK/PD verilerle tedaviler
- Hastaya özgün tedaviler
- Karbapenem alternatiflerinin daha etkin kullanımı

  Karbapenem kullanımında;

  Ertapenem ??? (ÜSİ, İAİ)
- Tigesiklin sadece endikasyonlarında ya da kombinasyonların bir üyesi olarak
- Kolistin çok dikkatli takip ile (kombine !)

SORUN BAKTERİLERLE MÜCADELE ELİMİZDEDİR